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(54) Title: PROTEIN KINASES

(57) Abstract: The present invention relates to novel kinase polypeptides, nucleotide sequences encoding the novel kinase polypep-  
tides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

DESCRIPTION

## PROTEIN KINASES

FIELD OF THE INVENTION

5           The present invention relates to novel kinase polypeptides, nucleotide sequences encoding the novel kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

BACKGROUND OF THE INVENTION

10           The following description of the background of the invention is provided to aid in understanding the invention, but is not admitted to be or to describe prior art to the invention.

          Cellular signal transduction is a fundamental mechanism whereby external stimuli that regulate diverse cellular processes are relayed to the interior of cells. One of the key  
15           biochemical mechanisms of signal transduction involves the reversible phosphorylation of proteins, which enables regulation of the activity of mature proteins by altering their structure and function.

          Protein phosphorylation plays a pivotal role in biological signal transduction. Among the biological functions controlled by protein phosphorylation are the following:  
20           cell division; differentiation and death (apoptosis); cell motility and cytoskeletal structure; control of DNA replication, transcription, splicing and translation; protein translocation events from the endoplasmic reticulum and Golgi apparatus to the membrane and extracellular space; protein nuclear import and export; regulation of metabolic reactions, etc. Abnormal protein phosphorylation is widely recognized to be causally linked to the  
25           etiology of many diseases including cancer as well as immunologic, neuronal and metabolic disorders.

          The most common phospho-acceptor amino acid residues are serine, threonine and tyrosine. Phosphorylation in histidine has also been observed in bacteria. The presence of a phosphate moiety modulates protein function in multiple ways. A common mechanism  
30           includes changes in the catalytic properties ( $V_{max}$  and  $K_m$ ) of an enzyme leading to its activation or inactivation. A second widely recognized mechanism involves promoting protein-protein interactions. An example of this is the tyrosine autophosphorylation of the



ligand-activated EGF receptor tyrosine kinase. This event triggers the high-affinity binding to the phosphotyrosine residue on the receptor's C-terminal intracellular domain to the SH2 motif of the adaptor molecule Grb2. Grb2 in turn binds through its SH3 motif to a second adaptor molecule, such as SHC. The formation of this ternary complex  
5 activates the signaling events that are responsible for the biological effects of EGF. Serine and threonine phosphorylation events have also been recently recognized to exert their biological function through protein-protein interaction events mediated by the high-affinity binding of phosphoserine and phosphothreonine to WW motifs present in a large variety of proteins (Lu, P.J. *et al.* (1999) *Science* 283:1325-1328). A third important  
10 outcome of protein phosphorylation is changes in the subcellular localization of the substrate. As an example, nuclear import and export events in a large diversity of proteins are regulated by protein phosphorylation (Drier E.A. *et al.* (1999) *Genes Dev* 13: 556-568).

Protein kinases are one of the largest families of eukaryotic proteins with several  
15 hundred known members. These proteins share a 250-300 amino acid domain that can be subdivided into 12 distinct subdomains that comprise the common catalytic core structure. These conserved protein motifs have recently been exploited using PCR-based and bioinformatic strategies leading to a significant expansion of the known kinases. Multiple  
20 alignment of the sequences in the catalytic domain of protein kinases and subsequent parsimony analysis permits their segregation into a dendrogram reflecting the relatedness of their catalytic domains (Fig. 1). In this manner, related kinases are clustered into distinct branches or subfamilies including: tyrosine kinases, cyclic-nucleotide-dependent kinases, calcium/calmodulin kinases, cyclin-dependent kinases and MAP-kinases, serine-threonine kinase receptors, and several other less defined subfamilies.

25 We have recently completed a systematic analysis of the protein kinases present in *C. elegans*, the multicellular organism whose entire DNA sequence has been determined. We identified 473 unique kinase profiles including 398 full-length conventional kinases, and 20 additional proteins that may function as atypical protein kinases. (Plowman G.D. *et al.* (1999), *Proc. Natl. Acad. Sci.* 96:13603-13610).

30 Using parsimony analysis, the protein kinases may be divided into 4 major groups: AGC, CAMK, CMGC and tyrosine kinases. In addition, there are a number of minor yet distinct families, including the STE and casein kinase 1, families related to worm- or

fungal-specific kinases, and a family designated "other" to represent several smaller families. In addition, we designate an "atypical" family to represent protein kinases whose catalytic domain has little or no primary sequence homology to conventional kinases, including the A6 kinases and PI3 kinases.

5       The AGC kinases are basic amino acid-directed enzymes that phosphorylate residues found proximal to Arg and Lys. Examples of this group are the cyclic nucleotide-dependent kinases, G protein kinases, NDR or DBF2 and the ribosomal S6 kinases.

10       The CAMK group kinases are also basic amino acid-directed kinases. They include the Ca<sup>2+</sup>/calmodulin-regulated and AMP-dependent protein kinases, myosin light chain kinases, checkpoint 2 kinases (CHK2) and EMK-related protein kinases. The EMK family of STK are involved in the control of cell polarity, microtubule stability and cancer. One member of the EMK family, C-TAK1 has been reported to control entry into mitosis by activating Cdc25C which in turn dephosphorylates Cdc2.

15       CMGC group kinases are "proline-directed" enzymes phosphorylating residues that exist in a proline-rich context. They include the cyclin-dependent kinases (CDKs), mitogen-activated kinases (MAPKs), GSK3s and CLKs. Most CMGC kinases have larger-than-average kinase domains owing to the presence of insertions within subdomains X and XI.

20       The tyrosine kinase group encompass both cytoplasmic (i.e. src) as well as transmembrane receptor tyrosine kinases (i.e. EGF receptor). These kinases play a pivotal role in the signal transduction processes that mediate cell proliferation, differentiation and apoptosis.

25       Group members that define smaller, yet distinct phylogenetic branches of conventional kinases include the elongation factor 2 kinases (EIFKs); homologues of the yeast sterile family kinases (STE) which refers to 3 classes of kinases which lie sequentially upstream of the MAPKs; mixed lineage kinases (MLKs); Lim-domain containing kinases (LIMKs); Calcium-calmodulin kinase kinases (CAMKK), dual-specific tyrosine kinases (DYRK), integrin receptor associated kinase (IRAK); testis-specific kinases (TSK); UNC-51 related kinases (UNC); several families that are close  
30       homologues to worm (C26C2.1, YQ09, ZC581.9, YFL033c, C24A1.3), Drosophila (SLOB), or yeast (YDOD\_sp, YGR262\_sc) kinases, and others that are "unique" and don't cluster into any obvious family.

### SUMMARY OF THE INVENTION

Through a search of the EST database for homologies to the conserved catalytic kinase domain of protein kinases, hundreds of mammalian members of known and previously unidentified protein kinase families and groups have been identified as part of the present invention. Multiple alignment and parsimony analysis of the catalytic domain reveals that approximately half of these protein kinases cluster into 10 known groups, with the other half perhaps defining novel groups. Classification in this manner has proven highly accurate not only in predicting motifs present in the remaining non-catalytic portion of each protein, but also in their regulation, substrates, and signaling pathways. The present invention includes the partial or complete sequence of new protein kinases, their classification, predicted or deduced protein structure, and a strategy for elucidating their biologic and therapeutic relevance.

Thus, a first aspect of the invention features an isolated, enriched, or purified nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,

SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
5 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
and SEQ ID NO:242.

By "isolated" in reference to nucleic acid is meant a polymer of nucleotides  
conjugated to each other, including DNA and RNA, that is isolated from a natural source  
10 or that is synthesized. The isolated nucleic acid of the present invention is unique in the  
sense that it is not found in a pure or separated state in nature. Use of the term "isolated"  
indicates that a naturally occurring sequence has been removed from its normal cellular  
(i.e., chromosomal) environment. Thus, the sequence may be in a cell-free solution or  
placed in a different cellular environment. The term does not imply that the sequence is  
15 the only nucleotide chain present, but that it is essentially free (about 90 - 95% pure at  
least) of non-nucleotide material naturally associated with it, and thus is distinguished  
from isolated chromosomes.

By the use of the term "enriched" in reference to nucleic acid is meant that the  
specific DNA or RNA sequence constitutes a significantly higher fraction (2 - 5 fold) of  
20 the total DNA or RNA present in the cells or solution of interest than in normal or  
diseased cells or in the cells from which the sequence was taken. This could be caused by  
a person by preferential reduction in the amount of other DNA or RNA present, or by a  
preferential increase in the amount of the specific DNA or RNA sequence, or by a  
combination of the two. However, it should be noted that enriched does not imply that  
25 there are no other DNA or RNA sequences present, just that the relative amount of the  
sequence of interest has been significantly increased. The term "significant" is used to  
indicate that the level of increase is useful to the person making such an increase, and  
generally means an increase relative to other nucleic acids of about at least 2 fold, more  
preferably at least 5 to 10 fold or even more. The term also does not imply that there is no  
30 DNA or RNA from other sources. The other source DNA may, for example, comprise  
DNA from a yeast or bacterial genome, or a cloning vector such as pUC19. This term  
distinguishes from naturally occurring events, such as viral infection, or tumor type

growths, in which the level of one mRNA may be naturally increased relative to other species of mRNA. That is, the term is meant to cover only those situations in which a person has intervened to elevate the proportion of the desired nucleic acid.

It is also advantageous for some purposes that a nucleotide sequence be in purified form. The term "purified" in reference to nucleic acid does not require absolute purity (such as a homogeneous preparation). Instead, it represents an indication that the sequence is relatively more pure than in the natural environment (compared to the natural level this level should be at least 2-5 fold greater, *e.g.*, in terms of mg/mL). Individual clones isolated from a cDNA library may be purified to electrophoretic homogeneity. The claimed DNA molecules obtained from these clones could be obtained directly from total DNA or from total RNA. The cDNA clones are not naturally occurring, but rather are preferably obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The construction of a cDNA library from mRNA involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection of the cells carrying the cDNA library. Thus, the process which includes the construction of a cDNA library from mRNA and isolation of distinct cDNA clones yields an approximately  $10^6$ -fold purification of the native message. Thus, purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

By a "kinase polypeptide" is meant 10 (preferably 20, more preferably 40, most preferably 75) or more contiguous amino acids set forth in an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,

SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178,  
SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183,  
SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188,  
SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193,  
5 SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
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SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
10 SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228,  
SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or functional  
15 derivatives thereof as described herein. For sequences for which the full-length sequence  
is not given, the remaining sequences can be determined using methods well-known to  
those in the art and are intended to be included in the invention. In certain aspects,  
polypeptides of 100, 200, 300 or more amino acids are preferred. The kinase polypeptide  
can be encoded by a full-length nucleic acid sequence or any portion of the full-length  
20 nucleic acid sequence, so long as a functional activity of the polypeptide is retained. By  
“functional” domain is meant any region of the polypeptide that may play a regulatory or  
catalytic role as predicted from amino acid sequence homology to other proteins or by the  
presence of amino acid sequences that may give rise to specific structural conformations  
(i.e., coiled-coils). For some purposes, polypeptide domains are preferred, including, but  
25 not limited to, N-terminal, catalytic/kinase and C-terminal.

The amino acid sequence will be substantially similar to a sequence selected from  
the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID  
NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID  
NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID  
30 NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID  
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15 NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID  
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NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID  
NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID  
NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding  
20 full-length amino acid sequence, or fragments thereof. A sequence that is substantially  
similar to a sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
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ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 or portions of or the entire corresponding full-length amino acid sequences.

By "identity" is meant a property of sequences that measures their similarity or relationship. Identity is measured by dividing the number of identical residues between two sequences (either full-length or a defined domain) by the total number of residues in the known sequence, or the domain of the known sequence, and multiplying the product by 100. Thus, two copies of exactly the same sequence have 100% identity, but sequences that are less highly conserved, and have replacements and substitutions, have a lower degree of identity. "Gaps" are spaces in an alignment that can result from aligning a novel sequence with a known sequence when the novel sequence has additions or deletions of amino acids in comparison with the known sequence. These gaps do not factor into the assessment of % identity using the above calculation.

Those skilled in the art will recognize that several computer programs are also available for determining sequence identity using standard parameters, for example, Blast (Altschul, *et al.* (1997) *Nucleic Acids Res.* 25:3389-3402), Blast2 (Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-410), and Smith-Waterman (Smith, *et al.* (1981) *J. Mol. Biol.* 147:195-197).

In preferred embodiments, the invention features isolated, enriched, or purified nucleic acid molecules encoding a kinase polypeptide comprising a nucleotide sequence that: (a) encodes a polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ

ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID

NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID

NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally occurring kinase polypeptide; (d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID

NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof.

A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence of SEQ ID

NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of a domain selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; (e) is the complement of the nucleotide sequence of (d); (f) encodes a polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID

NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. (The domain demarcations of the polypeptides of the invention are indicated in Table 2 by reference to the kinase domain.) A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID

NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ



ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally occurring kinase polypeptide; (d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID

NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof.

A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235,

SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to a domain of a polypeptide selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, where the domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; (g) is the complement of the nucleotide sequence of (f); (h) encodes a polypeptide having an amino acid sequence selected from the group consisting

of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,

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10 SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
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SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
15 SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
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SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at  
20 least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-  
100%) to the sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
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NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID  
NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID  
NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID  
30 NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID  
NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID  
NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID

NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID  
NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID  
NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID  
NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID  
5 NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID  
NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID  
NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID  
NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID  
NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID  
10 NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID  
NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID  
NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID  
NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c) hybridizes under  
15 highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally  
occurring kinase polypeptide; (d) encodes a kinase polypeptide having an amino acid  
sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID  
NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID  
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20 NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID  
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30 NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID  
NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID  
NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID

NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,

SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more of the domains selected from the group consisting of a N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; or (i) is the



complement of the nucleotide sequence of (h). The domain demarcations of the polypeptides of the invention are indicated in Table 2 by reference to the kinase domain.

The term "complement" refers to two nucleotides that can form multiple favorable interactions with one another. For example, adenine is complementary to thymine as they can form two hydrogen bonds. Similarly, guanine and cytosine are complementary since they can form three hydrogen bonds. A nucleotide sequence is the complement of another nucleotide sequence if all of the nucleotides of the first sequence are complementary to all of the nucleotides of the second sequence.

The term "domain" refers to a region of a polypeptide that contains a particular function. For instance, N-terminal or C-terminal domains of signal transduction proteins can serve functions including, but not limited to, binding molecules that localize the signal transduction molecule to different regions of the cell or binding other signaling molecules directly responsible for propagating a particular cellular signal. Some domains can be expressed separately from the rest of the protein and function by themselves, while others must remain part of the intact protein to retain function. The latter are termed functional regions of proteins and also relate to domains.

The term "N-terminal domain" refers to the extracatalytic region located between the initiator methionine and the catalytic domain of the protein kinase. The N-terminal domain can be identified following a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the N-terminal boundary of the catalytic domain. Depending on its length, the N-terminal domain may or may not play a regulatory role in kinase function. An example of a protein kinase whose N-terminal domain has been shown to play a regulatory role is PAK65, which contains a CRIB motif used for Cdc42 and rac binding (Burbelo, P.D. *et al.* (1995) J. Biol. Chem. 270, 29071-29074). The N-terminal domain of a protein kinase of the invention is that portion of the protein kinase to the amino-terminal side of the kinase domain where the kinase domain is identified in Table 2, herein. Further, in some cases, portions of the N-terminal domains of the protein kinases of the invention have not been identified since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined and using the approaches described herein the N-terminal domain can be identified.

The term "catalytic domain" or "kinase domain" refers to a region of the protein kinase that is typically 25-300 amino acids long and is responsible for carrying out the phosphate transfer reaction from a high-energy phosphate donor molecule such as ATP or GTP to itself (autophosphorylation) or to other proteins (exogenous phosphorylation).

5 The catalytic domain of protein kinases is made up of 12 subdomains that contain highly conserved amino acid residues, and are responsible for proper polypeptide folding and for catalysis. The catalytic domain can be identified following a Smith-Waterman alignment of the protein sequence against the non-redundant protein database. The catalytic/kinase domains of the protein kinases of the invention are identified in Table 2, herein. Further,  
10 in some cases, the complete sequence of the catalytic/kinase domains of the protein kinases of the invention may not have been provided since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined, and using the approaches described herein, the catalytic/kinase domain can be identified.

15 The term "catalytic activity", as used herein, defines the rate at which a kinase catalytic domain phosphorylates a substrate. Catalytic activity can be measured, for example, by determining the amount of a substrate converted to a phosphorylated product as a function of time. Catalytic activity can be measured by methods of the invention by holding time constant and determining the concentration of a phosphorylated substrate  
20 after a fixed period of time. Phosphorylation of a substrate occurs at the active-site of a protein kinase. The active-site is normally a cavity in which the substrate binds to the protein kinase and is phosphorylated.

The term "substrate" as used herein refers to a molecule phosphorylated by a kinase of the invention. Kinases phosphorylate substrates on serine/threonine or tyrosine  
25 amino acids. The molecule may be another protein or a polypeptide.

The term "C-terminal domain" refers to the region located between the catalytic domain and the carboxy-terminal amino acid residue of the protein kinase. The C-terminal domain can be identified by using a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the C-terminal boundary of  
30 the catalytic domain or of any functional C-terminal extracatalytic domain. Depending on its length and amino acid composition, the C-terminal domain may or may not play a regulatory role in kinase function. An example of a protein kinase whose C-terminal

domain may play a regulatory role is PAK3 which contains a heterotrimeric G<sub>i</sub> subunit-binding site near its C-terminus (Leeuw, T. *et al.* (1998) *Nature*, 391, 191-195). The C-terminal domain of a protein kinase of the invention is that portion of the protein kinase to the carboxy-terminal side of the kinase domain where the kinase domain is identified in Table 2, herein. In some cases, the C-terminal domains of the protein kinases of the invention have not been provided since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined, and using the approaches described herein, the C-terminal domain can be identified.

The term "signal transduction pathway" refers to the molecules that propagate an extracellular signal through the cell membrane to become an intracellular signal. This signal can then stimulate a cellular response. The polypeptide molecules involved in signal transduction processes are typically receptor and non-receptor protein tyrosine kinases, receptor and non-receptor protein phosphatases, SRC homology 2 and 3 domains, phosphotyrosine binding proteins (SRC homology 2 (SH2) and phosphotyrosine binding (PTB and PH) domain containing proteins), proline-rich binding proteins (SH3 domain containing proteins), nucleotide exchange factors, and transcription factors.

The term "coiled-coil structure region" as used herein, refers to a polypeptide sequence that has a high probability of adopting a coiled-coil structure as predicted by computer algorithms such as COILS (Lupas, A. (1996) *Meth. Enzymology* 266:513-525). Coiled-coils are formed by two or three amphipathic  $\alpha$ -helices in parallel. Coiled-coils can bind to coiled-coil domains of other polypeptides resulting in homo- or heterodimers (Lupas, A. (1991) *Science* 252:1162-1164). Coiled-coil-dependent oligomerization has been shown to be necessary for protein function including catalytic activity of serine/threonine kinases (Roe, J. *et al.* (1997) *J. Biol. Chem.* 272:5838-5845). Coiled-coil regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "proline-rich region" as used herein, refers to a region of a protein kinase whose proline content over a given amino acid length is higher than the average content of this amino acid found in proteins (*i.e.*, >10%). Proline-rich regions are easily discernable by visual inspection of amino acid sequences and quantitated by standard computer

sequence analysis programs such as the DNASTar program EditSeq. Proline-rich regions have been demonstrated to participate in regulatory protein-protein interactions. Among these interactions, those that are most relevant to this invention involve the "PxxP" proline rich motif found in certain protein kinases (*i.e.*, human PAK1) and the SH3 domain of the adaptor molecule Nck (Galisteo, M.L. *et al.* (1996) J. Biol. Chem. 271:20997-21000).  
5 Other regulatory interactions involving "PxxP" proline-rich motifs include the WW domain (Sudol, M. (1996) Prog. Biophys. Mol. Bio. 65:113-132). Proline rich regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of  
10 the invention.

The term "spacer region" as used herein, refers to a region of the protein kinase located between predicted functional domains. The spacer region has no detectable homology to any amino acid sequence in the database, and can be identified by using a Smith-Waterman alignment of the protein sequence against the non-redundant protein  
15 database to define the C- and N-terminal boundaries of the flanking functional domains. Spacer regions may or may not play a fundamental role in protein kinase function. Precedence for the regulatory role of spacer regions in kinase function is provided by the role of the src kinase spacer in inter-domain interactions (Xu, W. *et al.* (1997) Nature 385:595-602). Spacer regions in the proteins of the invention can be identified using these  
20 methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "insert" as used herein refers to a portion of a protein kinase that is absent from a close homolog. Inserts may or may not be the product alternative splicing of exons. Inserts can be identified by using a Smith-Waterman sequence alignment of the  
25 protein sequence against the non-redundant protein database, or by means of a multiple sequence alignment of homologous sequences using the DNASTar program Megalign. Inserts may play a functional role by presenting a new interface for protein-protein interactions, or by interfering with such interactions. Insert regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of  
30 the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "C-terminal tail" as used herein, refers to a C-terminal domain of a protein kinase, that by homology extends or protrudes past the C-terminal amino acid of its closest homolog. C-terminal tails can be identified by using a Smith-Waterman sequence alignment of the protein sequence against the non-redundant protein database, or by means of a multiple sequence alignment of homologous sequences using the DNASTar program Megalign. Depending on its length, a C-terminal tail may or may not play a regulatory role in kinase function. C-terminal tail regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

Various low or high stringency hybridization conditions may be used depending upon the specificity and selectivity desired. These conditions are well-known to those skilled in the art. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 20 contiguous nucleotides, more preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 50 contiguous nucleotides, most preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 100 contiguous nucleotides. In some instances, the conditions may prevent hybridization of nucleic acids having more than 5 mismatches in the full-length sequence.

By stringent hybridization assay conditions is meant hybridization assay conditions at least as stringent as the following: hybridization in 50% formamide, 5X SSC, 50 mM  $\text{NaH}_2\text{PO}_4$ , pH 6.8, 0.5% SDS, 0.1 mg/mL sonicated salmon sperm DNA, and 5X Denhart solution at 42 °C overnight; washing with 2X SSC, 0.1% SDS at 45 °C; and washing with 0.2X SSC, 0.1% SDS at 45 °C. Under some of the most stringent hybridization assay conditions, the second wash can be done with 0.1X SSC at a temperature up to 70 °C (pg. 421, Berger *et al.* (1987) Guide to Molecular Cloning Techniques, Meth. Enzym. vol. 152, hereby incorporated by reference herein including any figures, tables, or drawings.). However, other applications may require the use of conditions falling between these sets of conditions. Methods of determining the conditions required to achieve desired hybridizations are well-known to those with ordinary skill in the art, and are based on several factors, including but not limited to, the sequences to be hybridized and the samples to be tested.

In other preferred embodiments, the invention features isolated, enriched, or purified nucleic acid molecules encoding kinase polypeptides, further comprising a vector or promoter effective to initiate transcription in a host cell. The invention also features recombinant nucleic acid, preferably in a cell or an organism. The recombinant nucleic acid may contain a sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or a functional derivative thereof and a vector or a promoter effective to initiate transcription in a host cell. The recombinant nucleic acid can alternatively contain a transcriptional initiation region functional in a cell, a sequence complementary to an RNA sequence encoding a kinase polypeptide and a transcriptional termination region functional in a cell. Specific

vectors and host cell combinations are discussed herein. The recombinant nucleic acid can also contain the full-length sequence encoding the protein kinase, or a domain, for example.

The term "vector" relates to a single or double-stranded circular nucleic acid molecule that can be transfected into cells and replicated within or independently of a cell genome. A circular double-stranded nucleic acid molecule can be cut and thereby linearized upon treatment with restriction enzymes. An assortment of nucleic acid vectors, restriction enzymes, and the knowledge of the nucleotide sequences cut by restriction enzymes are readily available to those skilled in the art. A nucleic acid molecule encoding a kinase can be inserted into a vector by cutting the vector with restriction enzymes and ligating the two pieces together.

The term "transfecting" defines a number of methods to insert a nucleic acid vector or other nucleic acid molecules into a cellular organism. These methods involve a variety of techniques, such as treating the cells with high concentrations of salt, an electric field, detergent, or DMSO to render the outer membrane or wall of the cells permeable to nucleic acid molecules of interest or use of various viral transduction strategies.

The term "promoter" as used herein, refers to nucleic acid sequence needed for gene sequence expression. Promoter regions vary from organism to organism, but are well known to persons skilled in the art for different organisms. For example, in prokaryotes, the promoter region contains both the promoter (which directs the initiation of RNA transcription) as well as the DNA sequences which, when transcribed into RNA, will signal synthesis initiation. Such regions will normally include those 5'-non-coding sequences involved with initiation of transcription and translation, such as the TATA box, capping sequence, CAAT sequence, and the like.

In preferred embodiments, the isolated nucleic acid comprises, consists essentially of, or consists of a nucleic acid sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35,

SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ  
ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID  
NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51,  
SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ  
5 ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID  
NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67,  
SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ  
ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID  
NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83,  
10 SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ  
ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID  
NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99,  
SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104,  
SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109,  
15 SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114,  
SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119,  
SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequence, encodes  
an amino acid sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
20 NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID  
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID  
25 NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID  
NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID  
NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID  
NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID  
NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID  
30 NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID  
NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID  
NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID



NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, a functional derivative thereof, or at least 10, 20, 40, 50, 75, 100, 200, 300 or 500 contiguous amino acids of a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID

NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length sequences or derivatives thereof. The nucleic acid may be isolated from a natural source by cDNA cloning or by subtractive hybridization. The natural source may be mammalian, preferably human, blood, semen, or tissue, and the nucleic acid may be synthesized by the triester method or by using an automated DNA synthesizer.

The term "mammal" refers preferably to such organisms as mice, rats, rabbits, guinea pigs, sheep, and goats, more preferably to cats, dogs, monkeys, and apes, and most preferably to humans.

In yet other preferred embodiments, the nucleic acid is a conserved or unique region, for example those useful for: the design of hybridization probes to facilitate identification and cloning of additional polypeptides, the design of PCR probes to facilitate cloning of additional polypeptides, obtaining antibodies to polypeptide regions, and designing antisense oligonucleotides.

By "conserved nucleic acid regions", are meant regions present on two or more nucleic acids encoding a kinase polypeptide, to which a particular nucleic acid sequence can hybridize under lower stringency conditions. Examples of lower stringency conditions suitable for screening for nucleic acid encoding kinase polypeptides are provided in Berger *et al.* (1987) Guide to Molecular Cloning Techniques, Meth. Enzym. vol. 152, hereby incorporated by reference herein in its entirety, including any drawings, figures, or tables. Preferably, conserved regions differ by no more than 5 out of 20 nucleotides, even more preferably 2 out of 20 nucleotides or most preferably 1 out of 20 nucleotides.

By "unique nucleic acid region" is meant a sequence present in a nucleic acid coding for a kinase polypeptide that is not present in a sequence coding for any other naturally occurring polypeptide. Such regions preferably encode 10 (preferably 25, more preferably 50, most preferably 75) or more contiguous amino acids selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,

SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
5 SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
10 SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
15 SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
20 SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or functional derivatives thereof.  
25 In particular, a unique nucleic acid region is preferably of mammalian origin and  
preferably human.

A second aspect of the invention features a nucleic acid probe for the detection of  
nucleic acid encoding a kinase polypeptide in a sample, wherein said polypeptide is  
selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
30 SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,

SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
5 SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
10 SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
15 SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
20 SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. Preferably, the nucleic acid  
probe encodes a kinase polypeptide that is a fragment of the protein encoded by an amino  
acid sequence selected from the group consisting of those set forth in SEQ ID NO:122,  
SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127,  
25 SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132,  
SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137,  
SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142,  
SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147,  
SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152,  
30 SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157,  
SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162,  
SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167,

SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172,  
SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177,  
SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,  
SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,  
5 SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
10 SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
15 SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242, or the corresponding full-length amino acid sequences. The nucleic acid probe  
contains a nucleotide base sequence that will hybridize to a sequence selected from the  
group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ  
ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,  
20 SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ  
ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID  
NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25,  
SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ  
ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID  
25 NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41,  
SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ  
ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID  
NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57,  
SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ  
30 ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID  
NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73,  
SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ

ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequence, or a functional derivative thereof.

In preferred embodiments, the nucleic acid probe hybridizes to nucleic acid encoding at least 6, 12, 75, 90, 105, 120, 150, 200, 250, 300 or 350 contiguous amino acids of a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID

NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or functional derivatives thereof.

Methods for using the probes include detecting the presence or amount of kinase RNA in a sample by contacting the sample with a nucleic acid probe under conditions such that hybridization occurs and detecting the presence or amount of the probe bound to kinase RNA. The nucleic acid duplex formed between the probe and a nucleic acid sequence coding for a kinase polypeptide may be used in the identification of the sequence of the nucleic acid detected (Nelson *et al.*, in *Nonisotopic DNA Probe Techniques*, Academic Press, San Diego, Kricka, ed., p. 275, 1992, hereby incorporated by reference herein in its entirety, including any drawings, figures, or tables). Kits for performing such methods may be constructed to include a container means having disposed therein a nucleic acid probe.

In a third aspect, the invention describes a recombinant cell or tissue comprising a nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,

SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
5 SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
10 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
and SEQ ID NO:242. In such cells, the nucleic acid may be under the control of the  
genomic regulatory elements, or may be under the control of exogenous regulatory  
elements including an exogenous promoter. By "exogenous" it is meant a promoter that is  
15 not normally coupled *in vivo* transcriptionally to the coding sequence for the kinase  
polypeptides.

The polypeptide is preferably a fragment of the protein encoded by an amino acid  
sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID  
NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID  
20 NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID  
NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID  
NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID  
NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID  
NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID  
25 NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID  
NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID  
NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID  
NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID  
NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID  
30 NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID  
NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID  
NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID



NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence. By "fragment," is meant an amino acid sequence present in a kinase polypeptide. Preferably, such a sequence comprises at least 10, 20, 40, 50, 75, 100, 200, or 300 contiguous amino acids a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,

SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
5 SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or of the corresponding full-  
length amino acid sequence, or a functional derivative thereof.

In a fourth aspect, the invention features an isolated, enriched, or purified kinase  
polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ  
10 ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ  
ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ  
ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ  
ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ  
ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ  
15 ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ  
ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ  
ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ  
ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ  
ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ  
20 ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ  
ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ  
ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ  
ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ  
ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ  
25 ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ  
ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ  
ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ  
ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ  
ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ  
30 ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ  
ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ

ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

By "isolated" in reference to a polypeptide is meant a polymer of amino acids (2 or more amino acids) conjugated to each other, including polypeptides that are isolated from a natural source or that are synthesized. The isolated polypeptides of the present invention are unique in the sense that they are not found in a pure or separated state in nature. Use of the term "isolated" indicates that a naturally occurring sequence has been removed from its normal cellular environment. Thus, the sequence may be in a cell-free solution or placed in a different cellular environment. The term does not imply that the sequence is the only amino acid chain present, but that it is essentially free (about 90 - 95% pure at least) of non-amino acid material naturally associated with it.

By the use of the term "enriched" in reference to a polypeptide is meant that the specific amino acid sequence constitutes a significantly higher fraction (2 - 5 fold) of the total amino acid sequences present in the cells or solution of interest than in normal or diseased cells or in the cells from which the sequence was taken. This could be caused by a person by preferential reduction in the amount of other amino acid sequences present, or by a preferential increase in the amount of the specific amino acid sequence of interest, or by a combination of the two. However, it should be noted that enriched does not imply that there are no other amino acid sequences present, just that the relative amount of the sequence of interest has been significantly increased. The term significant here is used to indicate that the level of increase is useful to the person making such an increase, and generally means an increase relative to other amino acid sequences of about at least 2-fold, more preferably at least 5- to 10-fold or even more. The term also does not imply that there is no amino acid sequence from other sources. The other source of amino acid sequences may, for example, comprise amino acid sequence encoded by a yeast or bacterial genome, or a cloning vector such as pUC19. The term is meant to cover only those situations in which man has intervened to increase the proportion of the desired amino acid sequence.

It is also advantageous for some purposes that an amino acid sequence be in purified form. The term "purified" in reference to a polypeptide does not require absolute purity (such as a homogeneous preparation); instead, it represents an indication that the sequence is relatively purer than in the natural environment. Compared to the natural level

this level should be at least 2-5 fold greater (*e.g.*, in terms of mg/mL). Purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated. The substance is preferably free of contamination at a functionally significant level, for example 90%, 95%, or 99% pure.

5           In preferred embodiments, the kinase polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,  
10       SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161,  
15       SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
20       SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
25       SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
30       and SEQ ID NO:242, or the corresponding full-length amino acid sequences. Preferably, the kinase polypeptide contains at least 10, 20, 40, 50, 75, 100, 200, or 300 contiguous

amino acids a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or a functional derivative thereof.

In preferred embodiments, the kinase polypeptide comprises an amino acid sequence having (a) an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ

ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ  
ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ  
ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ  
ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ  
5 ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ  
ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ  
ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ  
ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ  
ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ  
10 ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ  
ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ  
ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ  
ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ  
ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ  
15 ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ  
ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ  
ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ  
ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ  
ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ  
20 ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ  
ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ  
ID NO:241, and SEQ ID NO:242; (b) an amino acid sequence selected from the group  
consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ  
ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ  
25 ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ  
ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ  
ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ  
ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ  
ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ  
30 ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ  
ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ  
ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ

ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of a domain selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; (c) an amino acid sequence of a domain of a polypeptide selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,

SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
5 SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
10 SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242 where the domain is selected from the group consisting of an N-terminal domain,  
a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich  
region, a spacer region, an insert, and a C-terminal tail; or (d) an amino acid sequence  
15 selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123,  
SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128,  
SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133,  
SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138,  
SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143,  
20 SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,  
SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153,  
SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158,  
SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163,  
SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168,  
25 SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,  
SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178,  
SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183,  
SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188,  
SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193,  
30 SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208,



SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213,  
SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228,  
5 SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it  
lacks one or more, but not all, of the domains selected from the group consisting of a C-  
terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich  
10 region, a coiled-coil structure region, an insert, and a C-terminal tail. (The domain  
demarcations of the polypeptides of the invention are indicated in Table 2 by reference to  
the kinase domain.)

The polypeptide can be isolated from a natural source by methods well-known in  
the art. The natural source may be mammalian, preferably human, blood, semen, or tissue,  
15 and the polypeptide may be synthesized using an automated polypeptide synthesizer. The  
isolated, enriched, or purified kinase polypeptide is preferably selected from the group  
consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ  
ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ  
ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ  
20 ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ  
ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ  
ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ  
ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ  
ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ  
25 ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ  
ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ  
ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ  
ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ  
ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ  
30 ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ  
ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ  
ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ

ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242A.

In some embodiments the invention includes a recombinant kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,

SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. By "recombinant kinase polypeptide" is meant a polypeptide produced by recombinant DNA techniques such that it is distinct from a naturally occurring polypeptide either in its location (*e.g.*, present in a different cell or tissue than found in nature), purity or structure. Generally, such a recombinant polypeptide will be present in a cell in an amount different from that normally observed in nature.

In a fifth aspect, the invention features an antibody (*e.g.*, a monoclonal or polyclonal antibody) having specific binding affinity to a kinase polypeptide or a kinase polypeptide domain or fragment where the polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ

ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. In preferred embodiments, the antibody binds specifically to domains of kinase polypeptides, that are defined *supra*.

By "specific binding affinity" is meant that the antibody binds to the target kinase polypeptide with greater affinity than it binds to other polypeptides under specified conditions. Antibodies or antibody fragments are polypeptides that contain regions that can bind other polypeptides. The term "specific binding affinity" describes an antibody that binds to a kinase polypeptide with greater affinity than it binds to other polypeptides under specified conditions.

The term "polyclonal" refers to antibodies that are heterogenous populations of antibody molecules derived from the sera of animals immunized with an antigen or an antigenic functional derivative thereof. For the production of polyclonal antibodies, various host animals may be immunized by injection with the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species.

"Monoclonal antibodies" are substantially homogenous populations of antibodies to a particular antigen. They may be obtained by any technique which provides for the production of antibody molecules by continuous cell lines in culture. Monoclonal antibodies may be obtained by methods known to those skilled in the art (Kohler *et al.*, Nature 256:495-497, 1975, and U.S. Patent No. 4,376,110, both of which are hereby incorporated by reference herein in their entirety including any figures, tables, or drawings).

The term "antibody fragment" refers to a portion of an antibody, often the hyper variable region and portions of the surrounding heavy and light chains, that displays specific binding affinity for a particular molecule. A hyper variable region is a portion of an antibody that physically binds to the polypeptide target.

Antibodies or antibody fragments having specific binding affinity to a kinase polypeptide or domains of a kinase polypeptide of the invention may be used in methods for detecting the presence and/or amount of kinase polypeptide in a sample by probing the sample with the antibody under conditions suitable for kinase-antibody immunocomplex formation and detecting the presence and/or amount of the antibody conjugated to the

kinase polypeptide. Diagnostic kits for performing such methods may be constructed to include antibodies or antibody fragments specific for the kinase as well as a conjugate of a binding partner of the antibodies or the antibodies themselves.

An antibody or antibody fragment with specific binding affinity to a kinase polypeptide of the invention can be isolated, enriched, or purified from a prokaryotic or eukaryotic organism. Routine methods known to those skilled in the art enable production of antibodies or antibody fragments, in both prokaryotic and eukaryotic organisms. Purification, enrichment, and isolation of antibodies, which are polypeptide molecules, are described above.

Antibodies having specific binding affinity to a kinase polypeptide of the invention may be used in methods for detecting the presence and/or amount of kinase polypeptide in a sample by contacting the sample with the antibody under conditions such that an immunocomplex forms and detecting the presence and/or amount of the antibody conjugated to the kinase polypeptide. Diagnostic kits for performing such methods may be constructed to include a first container containing the antibody and a second container having a conjugate of a binding partner of the antibody and a label, such as, for example, a radioisotope. The diagnostic kit may also include notification of an FDA approved use and instructions therefor.

In a sixth aspect, the invention features a hybridoma which produces an antibody having specific binding affinity to a kinase polypeptide or a kinase polypeptide domain, where the polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID

NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; and where the domains are defined as above. By "hybridoma" is meant an immortalized cell line that is capable of secreting an antibody, for example an antibody to a kinase of the invention. In preferred embodiments, the antibody to the kinase comprises a sequence of amino acids that is able to specifically bind a kinase polypeptide of the invention.

In a seventh aspect, the invention features a kinase polypeptide binding agent able to bind to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,

SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
5 SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
10 SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242. The binding agent is preferably a purified antibody that recognizes an epitope  
present on a kinase polypeptide of the invention. Other binding agents include molecules  
that bind to kinase polypeptides and analogous molecules that bind to a kinase  
15 polypeptide. Such binding agents may be identified by using assays that measure kinase  
binding partner activity, such as those that measure PDGFR activity.

The invention also features a method for screening for human cells containing a  
kinase polypeptide of the invention or an equivalent sequence. The method involves  
identifying the novel polypeptide in human cells using techniques that are routine and  
20 standard in the art, such as those described herein for identifying the kinases of the  
invention (*e.g.*, cloning, Southern or Northern blot analysis, in situ hybridization, PCR  
amplification, etc.).

In an eighth aspect, the invention features methods for identifying a substance that  
modulates kinase activity comprising the steps of: (a) contacting a kinase polypeptide  
25 selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
30 SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,

SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
5 SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
10 SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
15 SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 with a test substance; (b)  
measuring the activity of said polypeptide; and (c) determining whether said substance  
modulates the activity of said polypeptide.

20 The term “modulates” refers to the ability of a compound to alter the function of a  
kinase of the invention. A modulator preferably activates or inhibits the activity of a  
kinase of the invention.

The term “activates” refers to increasing the cellular activity of the kinase. The  
term inhibit refers to decreasing the cellular activity of the kinase. Kinase activity is  
25 preferably the interaction with a natural binding partner.

The term “modulates” also refers to altering the function of kinases of the  
invention by increasing or decreasing the probability that a complex forms between the  
kinase and a natural binding partner. A modulator preferably increases the probability that  
such a complex forms between the kinase and the natural binding partner, more preferably  
30 increases or decreases the probability that a complex forms between the kinase and the  
natural binding partner depending on the concentration of the compound exposed to the



kinase, and most preferably decreases the probability that a complex forms between the kinase and the natural binding partner.

The term “complex” refers to an assembly of at least two molecules bound to one another. Signal transduction complexes often contain at least two protein molecules bound to one another. For instance, a protein tyrosine receptor protein kinase, GRB2, SOS, RAF, and RAS assemble to form a signal transduction complex in response to a mitogenic ligand.

The term “natural binding partner” refers to polypeptides, lipids, small molecules, or nucleic acids that bind to kinases in cells. A change in the interaction between a kinase and a natural binding partner can manifest itself as an increased or decreased probability that the interaction forms, or an increased or decreased concentration of kinase/natural binding partner complex.

The term “contacting” as used herein refers to mixing a solution comprising the test compound with a liquid medium bathing the cells of the methods. The solution comprising the compound may also comprise another component, such as dimethyl sulfoxide (DMSO), which facilitates the uptake of the test compound or compounds into the cells of the methods. The solution comprising the test compound may be added to the medium bathing the cells by utilizing a delivery apparatus, such as a pipet-based device or syringe-based device.

In a ninth aspect, the invention features methods for identifying a substance that modulates kinase activity in a cell comprising the steps of: (a) expressing a kinase polypeptide in a cell, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171,

SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176,  
SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181,  
SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
5 SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
10 SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
15 and SEQ ID NO:242; (b) adding a test substance to said cell; and (c) monitoring a change  
in cell phenotype or the interaction between said polypeptide and a natural binding  
partner.

The term “expressing” as used herein refers to the production of kinases of the  
invention from a nucleic acid vector containing kinase genes within a cell. The nucleic  
20 acid vector is transfected into cells using well known techniques in the art as described  
herein.

In a tenth aspect, the invention provides methods for treating a disease or abnormal  
condition by administering to a patient in need of such treatment a substance that  
modulates the activity of a polypeptide selected from the group consisting of SEQ ID  
25 NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID  
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
30 NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID  
NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID  
NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID

NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. Preferably, the disease is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer. Also included are metabolic disorders, such as diabetes mellitus, and reproductive disorders, such as infertility.

Preferably, the disease or disorder is selected from the group consisting of rheumatoid arthritis, atherosclerosis, autoimmune disorders, and organ transplantation. Preferably the disease or disorder is selected from the group consisting of immune-related diseases and disorders, myocardial infarction, cardiomyopathies, stroke, renal failure, and oxidative stress-related neurodegenerative disorders. Most preferably, the immune-related diseases and disorders are selected from the group consisting of rheumatoid arthritis, chronic inflammatory bowel disease, chronic inflammatory pelvic disease, multiple sclerosis, asthma, osteoarthritis, psoriasis, atherosclerosis, rhinitis, autoimmunity, and organ transplantation.

Substances useful for treatment of disorders or diseases preferably show positive results in one or more in vitro assays for an activity corresponding to treatment of the disease or disorder in question. Substances that modulate the activity of the polypeptides

preferably include, but are not limited to, antisense oligonucleotides and inhibitors of protein kinases.

The term "preventing" refers to decreasing the probability that an organism contracts or develops an abnormal condition.

5       The term "treating" refers to having a therapeutic effect and at least partially alleviating or abrogating an abnormal condition in the organism.

10       The term "therapeutic effect" refers to the inhibition or activation factors causing or contributing to the abnormal condition. A therapeutic effect relieves to some extent one or more of the symptoms of the abnormal condition. In reference to the treatment of abnormal conditions, a therapeutic effect can refer to one or more of the following: (a) an increase in the proliferation, growth, and/or differentiation of cells; (b) inhibition (*i.e.*, slowing or stopping) of cell death; (c) inhibition of degeneration; (d) relieving to some extent one or more of the symptoms associated with the abnormal condition; and (e) enhancing the function of the affected population of cells. Compounds demonstrating efficacy against abnormal conditions can be identified as described herein.

15       The term "abnormal condition" refers to a function in the cells or tissues of an organism that deviates from their normal functions in that organism. An abnormal condition can relate to cell proliferation, cell differentiation or cell survival. An abnormal condition may also include irregularities in cell cycle progression, *i.e.*, irregularities in normal cell cycle progression through mitosis and meiosis.

20       Abnormal cell proliferative conditions include cancers such as fibrotic and mesangial disorders, abnormal angiogenesis and vasculogenesis, wound healing, psoriasis, diabetes mellitus, and inflammation.

25       Abnormal differentiation conditions include, but are not limited to neurodegenerative disorders, slow wound healing rates, and slow tissue grafting healing rates.

30       Abnormal cell survival conditions relate to conditions in which programmed cell death (apoptosis) pathways are activated or abrogated. A number of protein kinases are associated with the apoptosis pathways. Aberrations in the function of any one of the protein kinases could lead to cell immortality or premature cell death.

The term "aberration", in conjunction with the function of a kinase in a signal transduction process, refers to a kinase that is over- or under-expressed in an organism, mutated such that its catalytic activity is lower or higher than wild-type protein kinase activity, mutated such that it can no longer interact with a natural binding partner, is no longer modified by another protein kinase or protein phosphatase, or no longer interacts with a natural binding partner.

The term "administering" relates to a method of incorporating a compound into cells or tissues of an organism. The abnormal condition can be prevented or treated when the cells or tissues of the organism exist within the organism or outside of the organism. Cells existing outside the organism can be maintained or grown in cell culture dishes. For cells harbored within the organism, many techniques exist in the art to administer compounds, including (but not limited to) oral, parenteral, dermal, injection, and aerosol applications. For cells outside of the organism, multiple techniques exist in the art to administer the compounds, including (but not limited to) cell microinjection techniques, transformation techniques, and carrier techniques.

The abnormal condition can also be prevented or treated by administering a compound to a group of cells having an aberration in a signal transduction pathway to an organism. The effect of administering a compound on organism function can then be monitored. The organism is preferably a mouse, rat, rabbit, guinea pig, or goat, more preferably a monkey or ape, and most preferably a human.

In an eleventh aspect, the invention features methods for detection the expression of a polypeptide in a sample as a diagnostic tool for diseases or disorders, wherein the method comprises the steps of: (a) contacting the sample with a nucleic acid probe which hybridizes under hybridization assay conditions to a nucleic acid target region of a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ

ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, said probe comprising the nucleic acid sequence encoding the polypeptide, fragments thereof, and the complements of the sequences and fragments; and (b) detecting the presence or amount of the probe:target region hybrid as an indication of the disease.

In preferred embodiments of the invention, the disease or disorder is selected from the group consisting of rheumatoid arthritis, arteriosclerosis, autoimmune disorders, organ transplantation, myocardial infarction, cardiomyopathies, stroke, renal failure, oxidative stress-related neurodegenerative disorders, metabolic disorder including diabetes, reproductive disorders including infertility, and cancer.

The kinase "target region" is a nucleotide base sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID

NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequences, a functional derivative thereof, or a fragment thereof to which the nucleic acid probe will specifically hybridize. Specific hybridization indicates that in the presence of other nucleic acids the probe only hybridizes detectably with the kinase of the invention's target region. Putative target regions can be identified by methods well known in the art consisting of alignment and comparison of the most closely related sequences in the database.

In preferred embodiments the nucleic acid probe hybridizes to a kinase target region encoding at least 6, 12, 75, 90, 105, 120, 150, 200, 250, 300 or 350 contiguous amino acids of the sequence set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID

NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID  
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NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID  
NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID  
NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID  
NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID  
NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID  
NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID  
NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID  
NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID  
NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID  
NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID  
NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID  
NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID  
NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID  
NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID  
NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding  
full-length amino acid sequence, or a functional derivative thereof. Hybridization

conditions should be such that hybridization occurs only with the kinase genes in the  
presence of other nucleic acid molecules. Under stringent hybridization conditions only  
highly complementary nucleic acid sequences hybridize. Preferably, such conditions  
prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 20  
contiguous nucleotides. Such conditions are defined *supra*.

Hybridization conditions should be such that hybridization occurs only with the  
genes in the presence of other nucleic acid molecules. Under stringent hybridization  
conditions only highly complementary nucleic acid sequences hybridize. Preferably, such  
conditions prevent hybridization of nucleic acids having 1 or 2 mismatches out of 20  
contiguous nucleotides. Such conditions are defined *supra*.

The diseases for which detection of kinase genes in a sample could be diagnostic  
include diseases in which kinase nucleic acid (DNA and/or RNA) is amplified in  
comparison to normal cells. By "amplification" is meant increased numbers of kinase



DNA or RNA in a cell compared with normal cells. In normal cells, kinases are typically found as single copy genes. In selected diseases, the chromosomal location of the kinase genes may be amplified, resulting in multiple copies of the gene, or amplification. Gene amplification can lead to amplification of kinase RNA, or kinase RNA can be amplified in the absence of kinase DNA amplification.

“Amplification” as it refers to RNA can be the detectable presence of kinase RNA in cells, since in some normal cells there is no basal expression of kinase RNA. In other normal cells, a basal level of expression of kinase exists, therefore in these cases amplification is the detection of at least 1-2-fold, and preferably more, kinase RNA, compared to the basal level.

The diseases that could be diagnosed by detection of kinase nucleic acid in a sample preferably include cancers. The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

Another aspect of the invention involves a method of agonizing (stimulating) or antagonizing a target of the invention and a natural binding partner associated activity in a mammal comprising administering to said mammal an agonist or antagonist to one of the above disclosed polypeptides in an amount sufficient to effect said agonism or antagonism. A method of treating diseases in a mammal with an agonist or antagonist of the protein of the present invention activity comprising administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize associated functions is also encompassed in the present application.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein polypeptides. Some small organic molecules form a class of compounds that modulate the function of protein polypeptides. Examples of molecules that have been reported to inhibit the function of protein kinases include, but are not limited to, bis monocyclic, bicyclic or heterocyclic aryl compounds (PCT WO 92/20642, published

November 26, 1992 by Maguire *et al.*), vinylene-azaindole derivatives (PCT WO 94/14808, published July 7, 1994 by Ballinari *et al.*), 1-cyclopropyl-4-pyridyl-quinolones (U.S. Patent No. 5,330,992), styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S. Patent No. 5,302,606), certain quinazoline derivatives (EP Application No. 0 566 266 A1), seleoindoles and selenides (PCT WO 94/03427, published February 17, 1994 by Denny *et al.*), tricyclic polyhydroxylic compounds (PCT WO 92/21660, published December 10, 1992 by Dow), and benzylphosphonic acid compounds (PCT WO 91/15495, published October 17, 1991 by Dow *et al.*), all of which are incorporated by reference herein, including any drawings.

Compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous as therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein inhibitors only weakly inhibit function. In addition, many inhibit a variety of protein kinases and will therefore cause multiple side-effects as therapeutics for diseases.

Some indolinone compounds, however, form classes of acid resistant and membrane permeable organic molecules. WO 96/22976 (published August 1, 1996 by Ballinari *et al.*) describes hydrosoluble indolinone compounds that harbor tetralin, naphthalene, quinoline, and indole substituents fused to the oxindole ring. These bicyclic substituents are in turn substituted with polar groups including hydroxylated alkyl, phosphate, and ether substituents. U.S. Patent Application Serial Nos. 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187) and 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298) and International Patent Publication WO 96/22976, published August 1, 1996 by Ballinari *et al.*, all of which are incorporated herein by reference in their entirety, including any drawings, describe indolinone chemical libraries of indolinone compounds harboring other bicyclic moieties as well as monocyclic moieties fused to the oxindole ring. Applications 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187), 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon

& Lyon Docket No. 223/298), and WO 96/22976, published August 1, 1996 by Ballinari *et al.* teach methods of indolinone synthesis, methods of testing the biological activity of indolinone compounds in cells, and inhibition patterns of indolinone derivatives, both of which are incorporated by reference herein, including any drawings.

5           Other examples of substances capable of modulating kinase activity include, but are not limited to, tyrphostins, quinazolines, quinoxolines, and quinolines. The quinazolines, tyrphostins, quinolines, and quinoxolines referred to above include well known compounds such as those described in the literature. For example, representative  
10       publications describing quinazolines include Barker *et al.*, EPO Publication No. 0 520 722 A1; Jones *et al.*, U.S. Patent No. 4,447,608; Kabbe *et al.*, U.S. Patent No. 4,757,072; Kaul and Vougioukas, U.S. Patent No. 5, 316,553; Kreighbaum and Comer, U.S. Patent No. 4,343,940; Pegg and Wardleworth, EPO Publication No. 0 562 734 A1; Barker *et al.*, Proc. of Am. Assoc. for Cancer Research 32:327 (1991); Bertino, J.R., Cancer Research 3:293-304 (1979); Bertino, J.R., Cancer Research 9(2 part 1):293-304 (1979); Curtin *et al.*, Br. J. Cancer 53:361-368 (1986); Fernandes *et al.*, Cancer Research 43:1117-1123 (1983); Ferris  
15       *et al.* J. Org. Chem. 44(2):173-178; Fry *et al.*, Science 265:1093-1095 (1994); Jackman *et al.*, Cancer Research 51:5579-5586 (1981); Jones *et al.* J. Med. Chem. 29(6):1114-1118; Lee and Skibo, Biochemistry 26(23):7355-7362 (1987); Lemus *et al.*, J. Org. Chem. 54:3511-3518 (1989); Ley and Seng, Synthesis 1975:415-522 (1975); Maxwell *et al.*,  
20       Magnetic Resonance in Medicine 17:189-196 (1991); Mini *et al.*, Cancer Research 45:325-330 (1985); Phillips and Castle, J. Heterocyclic Chem. 17(19):1489-1596 (1980); Reece *et al.*, Cancer Research 47(11):2996-2999 (1977); Sculier *et al.*, Cancer Immunol. and Immunother. 23:A65 (1986); Sikora *et al.*, Cancer Letters 23:289-295 (1984); and Sikora *et al.*, Analytical Biochem. 172:344-355 (1988), all of which are incorporated  
25       herein by reference in their entirety, including any drawings.

Quinoxaline is described in Kaul and Vougioukas, U.S. Patent No. 5,316,553, incorporated herein by reference in its entirety, including any drawings.

Quinolines are described in Dolle *et al.*, J. Med. Chem. 37:2627-2629 (1994); MaGuire, J. Med. Chem. 37:2129-2131 (1994); Burke *et al.*, J. Med. Chem. 36:425-432  
30       (1993); and Burke *et al.* BioOrganic Med. Chem. Letters 2:1771-1774 (1992), all of which are incorporated by reference in their entirety, including any drawings.

Tyrphostins are described in Allen et al., Clin. Exp. Immunol. 91:141-156 (1993); Anafi et al., Blood 82:12:3524-3529 (1993); Baker et al., J. Cell Sci. 102:543-555 (1992); Bilder et al., Amer. Physiol. Soc. pp. 6363-6143:C721-C730 (1991); Brunton et al., Proceedings of Amer. Assoc. Cancer Rsch. 33:558 (1992); Bryckaert et al., Experimental  
5 Cell Research 199:255-261 (1992); Dong et al., J. Leukocyte Biology 53:53-60 (1993); Dong et al., J. Immunol. 151(5):2717-2724 (1993); Gazit et al., J. Med. Chem. 32:2344-2352 (1989); Gazit et al., "J. Med. Chem. 36:3556-3564 (1993); Kaur et al., Anti-Cancer Drugs 5:213-222 (1994); Kaur et al., King et al., Biochem. J. 275:413-418 (1991); Kuo et al., Cancer Letters 74:197-202 (1993); Levitzki, A., The FASEB J. 6:3275-3282 (1992);  
10 Lyall et al., J. Biol. Chem. 264:14503-14509 (1989); Peterson et al., The Prostate 22:335-345 (1993); Pillemer et al., Int. J. Cancer 50:80-85 (1992); Posner et al., Molecular Pharmacology 45:673-683 (1993); Rendu et al., Biol. Pharmacology 44(5):881-888 (1992); Sauro and Thomas, Life Sciences 53:371-376 (1993); Sauro and Thomas, J. Pharm. and Experimental Therapeutics 267(3):119-1125 (1993); Wolbring et al., J. Biol. Chem. 269(36):22470-22472 (1994); and Yoneda et al., Cancer Research 51:4430-4435  
15 (1991); all of which are incorporated herein by reference in their entirety, including any drawings.

Other compounds that could be used as modulators include oxindolinones such as those described in U.S. patent application Serial No. 08/702,232 filed August 23, 1996,  
20 incorporated herein by reference in its entirety, including any drawings.  
Methods of Treating a Disease (Enablement - i.e., Dosing)

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number  
25 WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being  
30 treated, the particular composition being used and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be

formulated in animal models to achieve a circulating concentration range that initially takes into account the  $IC_{50}$  as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors and major organs can also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows:

- 1) the compound is administered to mice (an untreated control mouse should also be used);
- 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and
- 3) the samples are analyzed for red and white blood cell counts, blood cell composition and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, Journal of American Veterinary Medical Assoc., 202:229-249, 1993).

Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness or toxicity. Gross abnormalities in tissue are noted and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

For the treatment of cancers the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness.

- 5 Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

In a final aspect, the invention features a method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein the method comprises: (a) comparing a nucleic acid target region encoding the kinase polypeptide in  
10 a sample, where the kinase polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
15 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID  
20 NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID  
25 NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID

NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or one or more fragments thereof, with a control nucleic acid target region encoding the kinase polypeptide, or one or more fragments thereof; and (b) detecting  
5 differences in sequence or amount between the target region and the control target region, as an indication of the disease or disorder. Preferably, the disease or disorder is selected from the group consisting of immune-related diseases and disorders, organ transplantation, myocardial infarction, cardiovascular disease, stroke, renal failure, oxidative stress-related neurodegenerative disorders, and cancer. Immune-related diseases and disorders include,  
10 but are not limited to, those discussed previously.

The term “comparing” as used herein refers to identifying discrepancies between the nucleic acid target region isolated from a sample, and the control nucleic acid target region. The discrepancies can be in the nucleotide sequences, *e.g.* insertions, deletions, or point mutations, or in the amount of a given nucleotide sequence. Methods to determine  
15 these discrepancies in sequences are well-known to one of ordinary skill in the art. The “control” nucleic acid target region refers to the sequence or amount of the sequence found in normal cells, *e.g.* cells that are not diseased as discussed previously.

The term also includes anti-sense molecules drawn thereto.

The invention has been described broadly and generically herein. Each of the  
20 narrower species and subgeneric groupings falling within the generic disclosure also form part of the invention. This includes the generic description of the invention with a proviso or negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein. For example, in some instances the nucleotide sequence of particular kinase polypeptides may not be part of a preferred  
25 embodiment.

The summary of the invention described above is not limiting and other features and advantages of the invention will be apparent from the following detailed description of the invention, and from the claims.

BRIEF DESCRIPTION OF THE FIGURES

Figures 1A to 1BB shows the amino acid sequences of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

Figures 2A to 2MMMM shows the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID



NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34,  
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ  
ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID  
NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50,  
5 SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ  
ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID  
NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66,  
SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ  
ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID  
10 NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82,  
SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ  
ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID  
NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98,  
SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103,  
15 SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108,  
SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113,  
SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118,  
SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121.

## DETAILED DESCRIPTION OF THE INVENTION

20 The present invention relates in part to kinase polypeptides, nucleic acids encoding  
such polypeptides, cells containing such nucleic acids, antibodies to such polypeptides,  
assays utilizing such polypeptides, and methods relating to all of the foregoing. The  
present invention is based upon the isolation and characterization of new kinase  
25 polypeptides. The polypeptides and nucleic acids may be produced using well-known and  
standard synthesis techniques when given the sequences presented herein.

### I. The Nucleic Acids of the Invention

30 Included within the scope of this invention are the functional equivalents of the  
herein-described isolated nucleic acid molecules. The degeneracy of the genetic code  
permits substitution of certain codons by other codons that specify the same amino acid  
and hence would give rise to the same protein. The nucleic acid sequence can vary

substantially since, with the exception of methionine and tryptophan, the known amino acids can be coded for by more than one codon. Thus, portions or all of the kinase genes of the invention could be synthesized to give a nucleic acid sequence significantly different from one selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121. The encoded amino acid sequence thereof would, however, be preserved.

In addition, the nucleic acid sequence may comprise a nucleotide sequence which results from the addition, deletion or substitution of at least one nucleotide to the 5'-end and/or the 3'-end of the nucleic acid sequence shown in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID

NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13,  
SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ  
ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID  
NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29,  
5 SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ  
ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID  
NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45,  
SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ  
ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID  
10 NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61,  
SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ  
ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID  
NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77,  
SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ  
15 ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID  
NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93,  
SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ  
ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID  
NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID  
20 NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID  
NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID  
NO:119, SEQ ID NO:120, and SEQ ID NO:121, or a derivative thereof. Any nucleotide  
or polynucleotide may be used in this regard, provided that its addition, deletion or  
substitution does not alter the amino acid sequence of SEQ ID NO:122, SEQ ID NO:123,  
25 SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128,  
SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133,  
SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138,  
SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143,  
SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,  
30 SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153,  
SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158,  
SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163,

SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168,  
SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,  
SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178,  
SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183,  
5 SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188,  
SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193,  
SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208,  
10 SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213,  
SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228,  
SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
15 SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, that is encoded  
by the nucleotide sequence. For example, the present invention is intended to include any  
nucleic acid sequence resulting from the addition of ATG as an initiation codon at the 5'-  
end of the inventive nucleic acid sequence or its derivative, or from the addition of TTA,  
20 TAG or TGA as a termination codon at the 3'-end of the inventive nucleotide sequence or  
its derivative. Moreover, the nucleic acid molecule of the present invention may, as  
necessary, have restriction endonuclease recognition sites added to its 5'-end and/or 3'-  
end.

Such functional alterations of a given nucleic acid sequence afford an opportunity  
25 to promote secretion and/or processing of heterologous proteins encoded by foreign  
nucleic acid sequences fused thereto, for example. All variations of the nucleotide  
sequence of the kinase genes of the invention and fragments thereof permitted by the  
genetic code are, therefore, included in this invention.

Further, it is possible to delete codons or to substitute one or more codons with  
30 codons other than degenerate codons to produce a structurally modified polypeptide, but  
one which has substantially the same utility or activity as the polypeptide produced by the  
unmodified nucleic acid molecule. As recognized in the art, the two polypeptides are

functionally equivalent, as are the two nucleic acid molecules that give rise to their production, even though the differences between the nucleic acid molecules are not related to the degeneracy of the genetic code. This is discussed further in the "Functional Derivatives" section, herein.

5           Finally, many of the nucleic acid molecules of the invention are provided as a partial sequence only (Fig. 2A through 2QQ). However, it is standard for one of ordinary skill in the art to obtain a full-length sequence when provided with a partial sequence. Similarly, when provided with a partial or full-length sequence it is standard for one of ordinary skill in the art to obtain nucleic acid sequence coding for homologous proteins.  
10           Therefore, these nucleic acid molecules are also part of the invention.

          The characteristics of the protein kinase nucleic acid sequences of the invention are provided in Table 1. The protein kinases fall into 10 known groups: AGC, CAMK, CKI, CMGC, dsPK, EIFK, LIMK, MLK, STE and TK. In addition, there are a significant number of protein kinases that do not belong to any of the known groups, and therefore  
15           presumably define new protein kinase groups.

          Additional characteristics may be found, *inter alia*, in the tables, namely Table 1, Table 2, Table 3 and Table 4, shown below.

## 20           II.    Nucleic Acid Probes, Methods, and Kits for Detection of Protein Kinases.

          A nucleic acid probe of the present invention may be used to probe an appropriate chromosomal or cDNA library by usual hybridization methods to obtain other nucleic acid molecules of the present invention. A chromosomal DNA or cDNA library may be prepared from appropriate cells according to recognized methods in the art (cf. "Molecular Cloning: A Laboratory Manual", second edition, Cold Spring Harbor Laboratory, .  
25           Sambrook, Fritsch, & Maniatis, eds., 1989).

          In the alternative, chemical synthesis can be carried out in order to obtain nucleic acid probes having nucleotide sequences that correspond to N-terminal, kinase or C-terminal portions, for example, of the amino acid sequence of the polypeptide of interest. The synthesized nucleic acid probes may be used as primers in a polymerase chain  
30           reaction (PCR) carried out in accordance with recognized PCR techniques, essentially according to PCR Protocols, "A Guide to Methods and Applications", Academic Press,

Michael, *et al.*, eds., 1990, utilizing the appropriate chromosomal or cDNA library to obtain the fragment of the present invention.

One skilled in the art can readily design such probes based on the sequence disclosed herein using methods of computer alignment and sequence analysis known in the art ("Molecular Cloning: A Laboratory Manual", 1989, *supra*). The hybridization probes of the present invention can be labeled by standard labeling techniques such as with a radiolabel, enzyme label, fluorescent label, biotin-avidin label, chemiluminescence, and the like. After hybridization, the probes may be visualized using known methods.

The nucleic acid probes of the present invention include RNA, as well as DNA probes, such probes being generated using techniques known in the art. The nucleic acid probe may be immobilized on a solid support. Examples of such solid supports include, but are not limited to, plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, and acrylic resins, such as polyacrylamide and latex beads. Techniques for coupling nucleic acid probes to such solid supports are well known in the art.

The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

One method of detecting the presence of nucleic acids of the invention in a sample comprises (a) contacting said sample with the above-described nucleic acid probe under conditions such that hybridization occurs, and (b) detecting the presence of said probe bound to said nucleic acid molecule. One skilled in the art would select the nucleic acid probe according to techniques known in the art as described above. Samples to be tested include but should not be limited to RNA samples of human tissue.

A kit for detecting the presence of nucleic acids of the invention in a sample comprises at least one container means having disposed therein the above-described nucleic acid probe. The kit may further comprise other containers comprising one or more of the following: wash reagents and reagents capable of detecting the presence of bound nucleic acid probe. Examples of detection reagents include, but are not limited to

radiolabelled probes, enzymatic labeled probes (horseradish peroxidase, alkaline phosphatase), and affinity labeled probes (biotin, avidin, or streptavidin).

In detail, a compartmentalized kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allow the efficient transfer of reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the probe or primers used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, and the like), and containers which contain the reagents used to detect the hybridized probe, bound antibody, amplified product, or the like. One skilled in the art will readily recognize that the nucleic acid probes described in the present invention can readily be incorporated into one of the established kit formats that are well known in the art.

### III. DNA Constructs Comprising a Protein Kinase Nucleic Acid Molecule and Cells Containing These Constructs.

The present invention also relates to a recombinant DNA molecule comprising, 5' to 3', a promoter effective to initiate transcription in a host cell and the above-described nucleic acid molecules. In addition, the present invention relates to a recombinant DNA molecule comprising a vector and an above-described nucleic acid molecule. The present invention also relates to a nucleic acid molecule comprising a transcriptional region functional in a cell, a sequence complementary to an RNA sequence encoding an amino acid sequence corresponding to the above-described polypeptide, and a transcriptional termination region functional in said cell. The above-described molecules may be isolated and/or purified DNA molecules.

The present invention also relates to a cell or organism that contains an above-described nucleic acid molecule and thereby is capable of expressing a polypeptide. The polypeptide may be purified from cells that have been altered to express the polypeptide. A cell is said to be "altered to express a desired polypeptide" when the cell, through genetic manipulation, is made to produce a protein which it normally does not produce or

which the cell normally produces at lower levels. One skilled in the art can readily adapt procedures for introducing and expressing either genomic, cDNA, or synthetic sequences into either eukaryotic or prokaryotic cells.

A nucleic acid molecule, such as DNA, is said to be "capable of expressing" a polypeptide if it contains nucleotide sequences which contain transcriptional and translational regulatory information and such sequences are "operably linked" to nucleotide sequences which encode the polypeptide. An operable linkage is a linkage in which the regulatory DNA sequences and the DNA sequence sought to be expressed are connected in such a way as to permit gene sequence expression. The precise nature of the regulatory regions needed for gene sequence expression may vary from organism to organism, but shall in general include a promoter region which, in prokaryotes, contains both the promoter (which directs the initiation of RNA transcription) as well as the DNA sequences which, when transcribed into RNA, will signal synthesis initiation. Such regions will normally include those 5'-non-coding sequences involved with initiation of transcription and translation, such as the TATA box, capping sequence, CAAT sequence, and the like.

If desired, the non-coding region 3' to the sequence encoding a kinase of the invention may be obtained by the above-described methods. This region may be retained for its transcriptional termination regulatory sequences, such as termination and polyadenylation. Thus, by retaining the 3'-region naturally contiguous to the DNA sequence encoding a kinase of the invention, the transcriptional termination signals may be provided. Where the transcriptional termination signals are not satisfactorily functional in the expression host cell, then a 3' region functional in the host cell may be substituted.

Two DNA sequences (such as a promoter region sequence and a sequence encoding a kinase of the invention) are said to be operably linked if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region sequence to direct the transcription of a gene sequence encoding a kinase of the invention, or (3) interfere with the ability of the gene sequence of a kinase of the invention to be transcribed by the promoter region sequence. Thus, a promoter region would be operably linked to a DNA sequence if the promoter were capable of effecting transcription of that DNA sequence.



Thus, to express a gene encoding a kinase of the invention, transcriptional and translational signals recognized by an appropriate host are necessary.

The present invention encompasses the expression of a gene encoding a kinase of the invention (or a functional derivative thereof) in either prokaryotic or eukaryotic cells. Prokaryotic hosts are, generally, very efficient and convenient for the production of recombinant proteins and are, therefore, one type of preferred expression system for kinases of the invention. Prokaryotes most frequently are represented by various strains of *E. coli*. However, other microbial strains may also be used, including other bacterial strains.

In prokaryotic systems, plasmid vectors that contain replication sites and control sequences derived from a species compatible with the host may be used. Examples of suitable plasmid vectors may include pBR322, pUC118, pUC119 and the like; suitable phage or bacteriophage vectors may include  $\gamma$ gt10,  $\gamma$ gt11 and the like; and suitable virus vectors may include pMAM-neo, pKRC and the like. Preferably, the selected vector of the present invention has the capacity to replicate in the selected host cell.

Recognized prokaryotic hosts include bacteria such as *E. coli*, *Bacillus*, *Streptomyces*, *Pseudomonas*, *Salmonella*, *Serratia*, and the like. However, under such conditions, the polypeptide will not be glycosylated. The prokaryotic host must be compatible with the replicon and control sequences in the expression plasmid.

To express a kinase of the invention (or a functional derivative thereof) in a prokaryotic cell, it is necessary to operably link the sequence encoding the kinase of the invention to a functional prokaryotic promoter. Such promoters may be either constitutive or, more preferably, regulatable (*i.e.*, inducible or derepressible). Examples of constitutive promoters include the *int* promoter of bacteriophage  $\lambda$ , the *bla* promoter of the  $\beta$ -lactamase gene sequence of pBR322, and the *cat* promoter of the chloramphenicol acetyl transferase gene sequence of pPR325, and the like. Examples of inducible prokaryotic promoters include the major right and left promoters of bacteriophage  $\lambda$  ( $P_L$  and  $P_R$ ), the *trp*, *recA*, *lacZ*, *lacI*, and *gal* promoters of *E. coli*, the  $\alpha$ -amylase (Ulmanen *et al.*, J. Bacteriol. 162:176-182, 1985) and the  $\zeta$ -28-specific promoters of *B. subtilis* (Gilman *et al.*, Gene Sequence 32:11-20, 1984), the promoters of the bacteriophages of *Bacillus* (Gryczan, In: The Molecular Biology of the Bacilli, Academic Press, Inc., NY, 1982), and *Streptomyces* promoters (Ward *et al.*, Mol. Gen. Genet. 203:468-478, 1986). Prokaryotic

promoters are reviewed by Glick (Ind. Microbiol. 1:277-282, 1987), Cenatiempo (Biochimie 68:505-516, 1986), and Gottesman (Ann. Rev. Genet. 18:415-442, 1984).

Proper expression in a prokaryotic cell also requires the presence of a ribosome-binding site upstream of the gene sequence-encoding sequence. Such ribosome-binding sites are disclosed, for example, by Gold *et al.* (Ann. Rev. Microbiol. 35:365-404, 1981). The selection of control sequences, expression vectors, transformation methods, and the like, are dependent on the type of host cell used to express the gene. As used herein, "cell", "cell line", and "cell culture" may be used interchangeably and all such designations include progeny. Thus, the words "transformants" or "transformed cells" include the primary subject cell and cultures derived therefrom, without regard to the number of transfers. It is also understood that all progeny may not be precisely identical in DNA content, due to deliberate or inadvertent mutations. However, as defined, mutant progeny have the same functionality as that of the originally transformed cell.

Host cells which may be used in the expression systems of the present invention are not strictly limited, provided that they are suitable for use in the expression of the kinase polypeptide of interest. Suitable hosts may often include eukaryotic cells. Preferred eukaryotic hosts include, for example, yeast, fungi, insect cells, mammalian cells either *in vivo*, or in tissue culture. Mammalian cells which may be useful as hosts include HeLa cells, cells of fibroblast origin such as VERO or CHO-K1, or cells of lymphoid origin and their derivatives. Preferred mammalian host cells include SP2/0 and J558L, as well as neuroblastoma cell lines such as IMR 332, which may provide better capacities for correct post-translational processing.

In addition, plant cells are also available as hosts, and control sequences compatible with plant cells are available, such as the cauliflower mosaic virus 35S and 19S, and nopaline synthase promoter and polyadenylation signal sequences. Another preferred host is an insect cell, for example the *Drosophila* larvae. Using insect cells as hosts, the *Drosophila* alcohol dehydrogenase promoter can be used (Rubin, Science 240:1453-1459, 1988). Alternatively, baculovirus vectors can be engineered to express large amounts of kinases of the invention in insect cells (Jasny, Science 238:1653, 1987; Miller *et al.*, In: Genetic Engineering, Vol. 8, Plenum, Setlow *et al.*, eds., pp. 277-297, 1986).

Any of a series of yeast expression systems can be utilized which incorporate promoter and termination elements from the actively expressed sequences coding for glycolytic enzymes that are produced in large quantities when yeast are grown in mediums rich in glucose. Known glycolytic gene sequences can also provide very efficient transcriptional control signals. Yeast provides substantial advantages in that it can also carry out post-translational modifications. A number of recombinant DNA strategies exist utilizing strong promoter sequences and high copy number plasmids which can be utilized for production of the desired proteins in yeast. Yeast recognizes leader sequences on cloned mammalian genes and secretes peptides bearing leader sequences (*i.e.*, pre-peptides). Several possible vector systems are available for the expression of kinases of the invention in a mammalian host.

A wide variety of transcriptional and translational regulatory sequences may be employed, depending upon the nature of the host. The transcriptional and translational regulatory signals may be derived from viral sources, such as adenovirus, bovine papilloma virus, cytomegalovirus, simian virus, or the like, where the regulatory signals are associated with a particular gene sequence which has a high level of expression. Alternatively, promoters from mammalian expression products, such as actin, collagen, myosin, and the like, may be employed. Transcriptional initiation regulatory signals may be selected which allow for repression or activation, so that expression of the gene sequences can be modulated. Of interest are regulatory signals which are temperature-sensitive so that by varying the temperature, expression can be repressed or initiated, or are subject to chemical (such as metabolite) regulation.

Expression of kinases of the invention in eukaryotic hosts requires the use of eukaryotic regulatory regions. Such regions will, in general, include a promoter region sufficient to direct the initiation of RNA synthesis. Preferred eukaryotic promoters include, for example, the promoter of the mouse metallothionein I gene sequence (Hamer *et al.*, J. Mol. Appl. Gen. 1:273-288, 1982); the TK promoter of Herpes virus (McKnight, Cell 31:355-365, 1982); the SV40 early promoter (Benoist *et al.*, Nature (London) 290:304-31, 1981); and the yeast gal4 gene sequence promoter (Johnston *et al.*, Proc. Natl. Acad. Sci. (USA) 79:6971-6975, 1982; Silver *et al.*, Proc. Natl. Acad. Sci. (USA) 81:5951-5955, 1984).

Translation of eukaryotic mRNA is initiated at the codon that encodes the first methionine. For this reason, it is preferable to ensure that the linkage between a eukaryotic promoter and a DNA sequence which encodes a kinase of the invention (or a functional derivative thereof) does not contain any intervening codons which are capable of encoding a methionine (*i.e.*, AUG). The presence of such codons results either in the formation of a fusion protein (if the AUG codon is in the same reading frame as the kinase of the invention coding sequence) or a frame-shift mutation (if the AUG codon is not in the same reading frame as the kinase of the invention coding sequence).

A nucleic acid molecule encoding a kinase of the invention and an operably linked promoter may be introduced into a recipient prokaryotic or eukaryotic cell either as a nonreplicating DNA or RNA molecule, which may either be a linear molecule or, more preferably, a closed covalent circular molecule. Since such molecules are incapable of autonomous replication, the expression of the gene may occur through the transient expression of the introduced sequence. Alternatively, permanent expression may occur through the integration of the introduced DNA sequence into the host chromosome.

A vector may be employed which is capable of integrating the desired gene sequences into the host cell chromosome. Cells which have stably integrated the introduced DNA into their chromosomes can be selected by also introducing one or more markers which allow for selection of host cells which contain the expression vector. The marker may provide for prototrophy to an auxotrophic host, biocide resistance, *e.g.*, antibiotics, or heavy metals, such as copper, or the like. The selectable marker gene sequence can either be directly linked to the DNA gene sequences to be expressed, or introduced into the same cell by co-transfection. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcription promoters, enhancers, and termination signals. cDNA expression vectors incorporating such elements include those described by Okayama (Mol. Cell. Biol. 3:280-, 1983).

The introduced nucleic acid molecule can be incorporated into a plasmid or viral vector capable of autonomous replication in the recipient host. Any of a wide variety of vectors may be employed for this purpose. Factors of importance in selecting a particular plasmid or viral vector include: the ease with which recipient cells that contain the vector may be recognized and selected from those recipient cells which do not contain the vector;

the number of copies of the vector which are desired in a particular host; and whether it is desirable to be able to "shuttle" the vector between host cells of different species.

Preferred prokaryotic vectors include plasmids such as those capable of replication in *E. coli* (such as, for example, pBR322, ColEI, pSC101, pACYC 184,  $\pi$ VX; "Molecular Cloning: A Laboratory Manual", 1989, *supra*). *Bacillus* plasmids include pC194, pC221, pT127, and the like (Gryczan, In: The Molecular Biology of the Bacilli, Academic Press, NY, pp. 307-329, 1982). Suitable *Streptomyces* plasmids include p1J101 (Kendall *et al.*, J. Bacteriol. 169:4177-4183, 1987), and streptomyces bacteriophages such as  $\phi$ C31 (Chater *et al.*, In: Sixth International Symposium on Actinomycetales Biology, Akademiai Kiado, Budapest, Hungary, pp. 45-54, 1986). *Pseudomonas* plasmids are reviewed by John *et al.* (Rev. Infect. Dis. 8:693-704, 1986), and Izaki (Jpn. J. Bacteriol. 33:729-742, 1978).

Preferred eukaryotic plasmids include, for example, BPV, vaccinia, SV40, 2-micron circle, and the like, or their derivatives. Such plasmids are well known in the art (Botstein *et al.*, Miami Wntr. Symp. 19:265-274, 1982; Broach, In: "The Molecular Biology of the Yeast *Saccharomyces*: Life Cycle and Inheritance", Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, p. 445-470, 1981; Broach, Cell 28:203-204, 1982; Bollon *et al.*, J. Clin. Hematol. Oncol. 10:39-48, 1980; Maniatis, In: Cell Biology: A Comprehensive Treatise, Vol. 3, Gene Sequence Expression, Academic Press, NY, pp. 563-608, 1980).

Once the vector or nucleic acid molecule containing the construct(s) has been prepared for expression, the DNA construct(s) may be introduced into an appropriate host cell by any of a variety of suitable means, *i.e.*, transformation, transfection, conjugation, protoplast fusion, electroporation, particle gun technology, calcium phosphate-precipitation, direct microinjection, and the like. After the introduction of the vector, recipient cells are grown in a selective medium, which selects for the growth of vector-containing cells. Expression of the cloned gene(s) results in the production of a kinase of the invention, or fragments thereof. This can take place in the transformed cells as such, or following the induction of these cells to differentiate (for example, by administration of bromodeoxyuracil to neuroblastoma cells or the like). A variety of incubation conditions can be used to form the peptide of the present invention. The most preferred conditions are those which mimic physiological conditions.

#### IV. The Proteins of the Invention

A variety of methodologies known in the art can be utilized to obtain the polypeptides of the present invention. The polypeptides may be purified from tissues or cells that naturally produce the polypeptides. Alternatively, the above-described isolated nucleic acid fragments could be used to express the kinases of the invention in any  
5 organism. The samples of the present invention include cells, protein extracts or membrane extracts of cells, or biological fluids. The samples will vary based on the assay format, the detection method, and the nature of the tissues, cells or extracts used as the sample.

10 Any eukaryotic organism can be used as a source for the polypeptides of the invention, as long as the source organism naturally contains such polypeptides. As used herein, "source organism" refers to the original organism from which the amino acid sequence of the subunit is derived, regardless of the organism the subunit is expressed in and ultimately isolated from.

15 One skilled in the art can readily follow known methods for isolating proteins in order to obtain the polypeptides free of natural contaminants. These include, but are not limited to: size-exclusion chromatography, HPLC, ion-exchange chromatography, and immuno-affinity chromatography.

Further, the polypeptides of the invention include the full-length polypeptides that  
20 can be identified from the full-length or partial sequences encoded by SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142,  
25 SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167,  
30 SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,

SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,  
SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
5 SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
10 SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242 (Figure 1). In addition, the polypeptides of the invention include the domains of  
these polypeptides, including, but not limited to, the N-terminal, kinase/catalytic, and C-  
15 terminal domains.

The characteristics of the protein kinase nucleic acid sequences of the invention are  
provided in Table 1. The protein kinases fall into 10 known groups: AGC, CAMK, CKI,  
CMGC, dsPK, EIFK, LIMK, MLK, STE and TK. In addition, there are a significant  
number of protein kinases that do not belong to any of the known groups, and therefore  
20 presumably define new protein kinase groups.

Additional characteristics are shown in, *inter alia*, the tables, namely Table 1,  
Table 2, Table 3 and Table 4, provided below.

#### V. Antibodies, Hybridomas, Methods of Use and Kits for Detection of Protein 25 Kinases

The present invention relates to an antibody having binding affinity to a kinase of  
the invention. The polypeptide may have an amino acid sequence selected from the group  
consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ  
ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ  
30 ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ  
ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ  
ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ

ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or a functional derivative thereof, or at least 9 contiguous amino acids thereof (preferably, at least 20, 30, 35, or 40 or more contiguous amino acids thereof). Alternatively, the antibody may bind to a part of the polypeptide not provided in the sequences above, but that is present in the full-length sequence of the polypeptide and that is easily obtained using methods standard in the art. Further, the antibody may bind specifically to particular domains of one or more of the kinases of the invention, including, but not limited to, the N-terminal, kinase/catalytic, or C-terminal domains.

The present invention also relates to an antibody having specific binding affinity to a kinase or kinase domain of the invention. Such an antibody may be isolated by comparing its binding affinity to a kinase of the invention with its binding affinity to other polypeptides. Those that bind selectively to a kinase of the invention would be chosen for use in methods requiring a distinction between a kinase of the invention and other



polypeptides. Such methods could include, but should not be limited to, the analysis of altered kinase expression in tissue containing other polypeptides.

The kinases of the present invention can be used in a variety of procedures and methods, such as for the generation of antibodies, for use in identifying pharmaceutical compositions, and for studying DNA/protein interaction.

The kinases of the present invention can be used to produce antibodies or hybridomas. One skilled in the art will recognize that if an antibody is desired, such a peptide could be generated as described herein and used as an immunogen. The antibodies of the present invention include monoclonal and polyclonal antibodies, as well fragments of these antibodies, and humanized forms. Humanized forms of the antibodies of the present invention may be generated using one of the procedures known in the art such as chimerization or CDR grafting.

The present invention also relates to a hybridoma that produces the above-described monoclonal antibody, or binding fragment thereof. A hybridoma is an immortalized cell line that is capable of secreting a specific monoclonal antibody.

In general, techniques for preparing monoclonal antibodies and hybridomas are well known in the art (Campbell, "Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology," Elsevier Science Publishers, Amsterdam, The Netherlands, 1984; St. Groth *et al.*, J. Immunol. Methods 35:1-21, 1980). Any animal (mouse, rabbit, and the like) which is known to produce antibodies can be immunized with the selected polypeptide. Methods for immunization are well known in the art. Such methods include subcutaneous or intraperitoneal injection of the polypeptide. One skilled in the art will recognize that the amount of polypeptide used for immunization will vary based on the animal that is immunized, the antigenicity of the polypeptide and the site of injection.

The polypeptide may be modified or administered in an adjuvant in order to increase the peptide antigenicity. Methods of increasing the antigenicity of a polypeptide are well known in the art. Such procedures include coupling the antigen with a heterologous protein (such as globulin or  $\beta$ -galactosidase) or through the inclusion of an adjuvant during immunization.

For monoclonal antibodies, spleen cells from the immunized animals are removed, fused with myeloma cells, such as SP2/0-Ag14 myeloma cells, and allowed to become monoclonal antibody producing hybridoma cells. Any one of a number of methods well known in the art can be used to identify the hybridoma cell that produces an antibody with the desired characteristics. These include screening the hybridomas with an ELISA assay, western blot analysis, or radioimmunoassay (Lutz *et al.*, Exp. Cell Res. 175:109-124, 1988). Hybridomas secreting the desired antibodies are cloned and the class and subclass are determined using procedures known in the art (Campbell, "Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology", *supra*, 1984).

For polyclonal antibodies, antibody-containing antisera is isolated from the immunized animal and is screened for the presence of antibodies with the desired specificity using one of the above-described procedures. The above-described antibodies may be detectably labeled. Antibodies can be detectably labeled through the use of radioisotopes, affinity labels (such as biotin, avidin, and the like), enzymatic labels (such as horse radish peroxidase, alkaline phosphatase, and the like) fluorescent labels (such as FITC or rhodamine, and the like), paramagnetic atoms, and the like. Procedures for accomplishing such labeling are well-known in the art, for example, *see* Stemberger *et al.*, J. Histochem. Cytochem. 18:315, 1970; Bayer *et al.*, Meth. Enzym. 62:308-, 1979; Engval *et al.*, Immunol. 109:129-, 1972; Goding, J. Immunol. Meth. 13:215-, 1976. The labeled antibodies of the present invention can be used for *in vitro*, *in vivo*, and *in situ* assays to identify cells or tissues that express a specific peptide.

The above-described antibodies may also be immobilized on a solid support. Examples of such solid supports include plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, acrylic resins and such as polyacrylamide and latex beads. Techniques for coupling antibodies to such solid supports are well known in the art (Weir *et al.*, "Handbook of Experimental Immunology" 4th Ed., Blackwell Scientific Publications, Oxford, England, Chapter 10, 1986; Jacoby *et al.*, Meth. Enzym. 34, Academic Press, N.Y., 1974). The immobilized antibodies of the present invention can be used for *in vitro*, *in vivo*, and *in situ* assays as well as in immunochromatography.

Furthermore, one skilled in the art can readily adapt currently available procedures, as well as the techniques, methods and kits disclosed herein with regard to antibodies, to generate peptides capable of binding to a specific peptide sequence in order to generate rationally designed antipeptide peptides (Hurby *et al.*, "Application of Synthetic Peptides: Antisense Peptides", In Synthetic Peptides, A User's Guide, W.H. Freeman, NY, pp. 289-307, 1992; Kaspczak *et al.*, Biochemistry 28:9230-9238, 1989).

Anti-peptide peptides can be generated by replacing the basic amino acid residues found in the peptide sequences of the kinases of the invention with acidic residues, while maintaining hydrophobic and uncharged polar groups. For example, lysine, arginine, and/or histidine residues are replaced with aspartic acid or glutamic acid and glutamic acid residues are replaced by lysine, arginine or histidine.

The present invention also encompasses a method of detecting a kinase polypeptide in a sample, comprising: (a) contacting the sample with an above-described antibody, under conditions such that immunocomplexes form, and (b) detecting the presence of said antibody bound to the polypeptide. In detail, the methods comprise incubating a test sample with one or more of the antibodies of the present invention and assaying whether the antibody binds to the test sample. Altered levels of a kinase of the invention in a sample as compared to normal levels may indicate disease.

Conditions for incubating an antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the antibody used in the assay. One skilled in the art will recognize that any one of the commonly available immunological assay formats (such as radioimmunoassays, enzyme-linked immunosorbent assays, diffusion based Ouchterlony, or rocket immunofluorescent assays) can readily be adapted to employ the antibodies of the present invention. Examples of such assays can be found in Chard ("An Introduction to Radioimmunoassay and Related Techniques" Elsevier Science Publishers, Amsterdam, The Netherlands, 1986), Bullock *et al.* ("Techniques in Immunocytochemistry," Academic Press, Orlando, FL Vol. 1, 1982; Vol. 2, 1983; Vol. 3, 1985), Tijssen ("Practice and Theory of Enzyme Immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology," Elsevier Science Publishers, Amsterdam, The Netherlands, 1985).

The immunological assay test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as blood, serum, plasma, or urine. The test samples used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is testable with the system utilized.

A kit contains all the necessary reagents to carry out the previously described methods of detection. The kit may comprise: (i) a first container means containing an above-described antibody, and (ii) second container means containing a conjugate comprising a binding partner of the antibody and a label. In another preferred embodiment, the kit further comprises one or more other containers comprising one or more of the following: wash reagents and reagents capable of detecting the presence of bound antibodies.

Examples of detection reagents include, but are not limited to, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the chromophoric, enzymatic, or antibody binding reagents that are capable of reacting with the labeled antibody. The compartmentalized kit may be as described above for nucleic acid probe kits. One skilled in the art will readily recognize that the antibodies described in the present invention can readily be incorporated into one of the established kit formats that are well known in the art.

#### VI. Isolation of Compounds That Interact With Protein Kinases

The present invention also relates to a method of detecting a compound capable of binding to a protein kinase of the invention, comprising incubating the compound with a kinase of the invention and detecting the presence of the compound bound to the kinase. The compound may be present within a complex mixture, for example, serum, body fluid, or cell extracts.

The present invention also relates to a method of detecting an agonist or antagonist of kinase activity or kinase binding partner activity comprising incubating cells that produce a kinase of the invention in the presence of a compound and detecting changes in the level of kinase activity or kinase binding partner activity. The compounds thus identified would produce a change in activity indicative of the presence of the compound.

The compound may be present within a complex mixture, for example, serum, body fluid, or cell extracts. Once the compound is identified it can be isolated using techniques well known in the art.

5 The present invention also encompasses a method of agonizing (stimulating) or antagonizing kinase associated activity in a mammal comprising administering to said mammal an agonist or antagonist to a kinase of the invention in an amount sufficient to effect said agonism or antagonism. A method of treating diseases in a mammal with an agonist or antagonist of kinase activity comprising administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize kinase associated functions  
10 is also encompassed in the present application.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein kinases. Some small organic molecules form a class of compounds that modulate the function of protein kinases. Examples of molecules that have been reported to inhibit  
15 the function of protein kinases include, but are not limited to, bis monocyclic, bicyclic or heterocyclic aryl compounds (PCT WO 92/20642, published November 26, 1992 by Maguire *et al.*), vinylene-azaindole derivatives (PCT WO 94/14808, published July 7, 1994 by Ballinari *et al.*), 1-cyclopropyl-4-pyridyl-quinolones (U.S. Patent No. 5,330,992), styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S.  
20 Patent No. 5,302,606), certain quinazoline derivatives (EP Application No. 0 566 266 A1), seleoindoles and selenides (PCT WO 94/03427, published February 17, 1994 by Denny *et al.*), tricyclic polyhydroxylic compounds (PCT WO 92/21660, published December 10, 1992 by Dow), and benzylphosphonic acid compounds (PCT WO 91/15495, published October 17, 1991 by Dow *et al.*).

25 Compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous as therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein kinase inhibitors only weakly inhibit the function of protein kinases. In addition, many inhibit a variety of protein kinases and will cause multiple side-effects as therapeutics for diseases.

30 Some indolinone compounds, however, form classes of acid resistant and membrane permeable organic molecules. WO 96/22976 (published August 1, 1996 by Ballinari *et al.*) describes hydrosoluble indolinone compounds that harbor tetralin,

naphthalene, quinoline, and indole substituents fused to the oxindole ring. These bicyclic substituents are in turn substituted with polar moieties including hydroxylated alkyl, phosphate, and ether moieties. U.S. Patent Application Serial Nos. 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187) and 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298) and International Patent Publication WO 96/22976, published August 1, 1996 by Ballinari *et al.*, all of which are incorporated herein by reference in their entirety, including any drawings, describe indolinone chemical libraries of indolinone compounds harboring other bicyclic moieties as well as monocyclic moieties fused to the oxindole ring. Applications 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187), 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298), and WO 96/22976, published August 1, 1996 by Ballinari *et al.* teach methods of indolinone synthesis, methods of testing the biological activity of indolinone compounds in cells, and inhibition patterns of indolinone derivatives.

Other examples of substances capable of modulating kinase activity include, but are not limited to, tyrphostins, quinazolines, quinoxolines, and quinolines. The quinazolines, tyrphostins, quinolines, and quinoxolines referred to above include well known compounds such as those described in the literature. For example, representative publications describing quinazolines include Barker *et al.*, EPO Publication No. 0 520 722 A1; Jones *et al.*, U.S. Patent No. 4,447,608; Kabbe *et al.*, U.S. Patent No. 4,757,072; Kaul and Vougioukas, U.S. Patent No. 5, 316,553; Kreighbaum and Comer, U.S. Patent No. 4,343,940; Pegg and Wardleworth, EPO Publication No. 0 562 734 A1; Barker *et al.*, Proc. of Am. Assoc. for Cancer Research 32:327 (1991); Bertino, J.R., Cancer Research 3:293-304 (1979); Bertino, J.R., Cancer Research 9(2 part 1):293-304 (1979); Curtin *et al.*, Br. J. Cancer 53:361-368 (1986); Fernandes *et al.*, Cancer Research 43:1117-1123 (1983); Ferris *et al.*, J. Org. Chem. 44(2):173-178; Fry *et al.*, Science 265:1093-1095 (1994); Jackman *et al.*, Cancer Research 51:5579-5586 (1981); Jones *et al.*, J. Med. Chem. 29(6):1114-1118; Lee and Skibo, Biochemistry 26(23):7355-7362 (1987); Lemus *et al.*, J.

Org. Chem. 54:3511-3518 (1989); Ley and Seng, Synthesis 1975:415-522 (1975); Maxwell *et al.*, Magnetic Resonance in Medicine 17:189-196 (1991); Mini *et al.*, Cancer Research 45:325-330 (1985); Phillips and Castle, J. Heterocyclic Chem. 17(19):1489-1596 (1980); Reece *et al.*, Cancer Research 47(11):2996-2999 (1977); Sculier *et al.*, Cancer Immunol. and Immunother. 23:A65 (1986); Sikora *et al.*, Cancer Letters 23:289-295 (1984); Sikora *et al.*, Analytical Biochem. 172:344-355 (1988); all of which are incorporated herein by reference in their entirety, including any drawings.

Quinoxaline is described in Kaul and Vougioukas, U.S. Patent No. 5,316,553, incorporated herein by reference in its entirety, including any drawings.

Quinolines are described in Dolle *et al.*, J. Med. Chem. 37:2627-2629 (1994); MaGuire, J. Med. Chem. 37:2129-2131 (1994); Burke *et al.*, J. Med. Chem. 36:425-432 (1993); and Burke *et al.*, BioOrganic Med. Chem. Letters 2:1771-1774 (1992), all of which are incorporated by reference in their entirety, including any drawings.

Tyrphostins are described in Allen *et al.*, Clin. Exp. Immunol. 91:141-156 (1993); Anafi *et al.*, Blood 82:12:3524-3529 (1993); Baker *et al.*, J. Cell Sci. 102:543-555 (1992); Bilder *et al.*, Amer. Physiol. Soc. pp. 6363-6143:C721-C730 (1991); Brunton *et al.*, Proceedings of Amer. Assoc. Cancer Rsch. 33:558 (1992); Bryckaert *et al.*, Experimental Cell Research 199:255-261 (1992); Dong *et al.*, J. Leukocyte Biology 53:53-60 (1993); Dong *et al.*, J. Immunol. 151(5):2717-2724 (1993); Gazit *et al.*, J. Med. Chem. 32:2344-2352 (1989); Gazit *et al.*, " J. Med. Chem. 36:3556-3564 (1993); Kaur *et al.*, Anti-Cancer Drugs 5:213-222 (1994); Kaur *et al.*, King *et al.*, Biochem. J. 275:413-418 (1991); Kuo *et al.*, Cancer Letters 74:197-202 (1993); Levitzki, A., The FASEB J. 6:3275-3282 (1992); Lyall *et al.*, J. Biol. Chem. 264:14503-14509 (1989); Peterson *et al.*, The Prostate 22:335-345 (1993); Pillemer *et al.*, Int. J. Cancer 50:80-85 (1992); Posner *et al.*, Molecular Pharmacology 45:673-683 (1993); Rendu *et al.*, Biol. Pharmacology 44(5):881-888 (1992); Sauro and Thomas, Life Sciences 53:371-376 (1993); Sauro and Thomas, J. Pharm. and Experimental Therapeutics 267(3):119-1125 (1993); Wolbring *et al.*, J. Biol. Chem. 269(36):22470-22472 (1994); and Yoneda *et al.*, Cancer Research 51:4430-4435 (1991); all of which are incorporated herein by reference in their entirety, including any drawings.

Other compounds that could be used as modulators include oxindolinones such as those described in U.S. patent application Serial No. 08/702,232 filed August 23, 1996, incorporated herein by reference in its entirety, including any drawings.

VII. Biological Significance, Applications and Clinical Relevance of Novel Protein  
5 Kinases

For each protein kinase in this application, we provide a classification of the protein class and family to which it belongs, a summary of non-catalytic protein motifs, a profile of its expression in several hundred tissue and cell sources, and a chromosomal location. This information can be used to suggest potential function, regulation or  
10 therapeutic utility for each of the proteins.

The kinase classification and protein domains often reflect pathways, cellular roles, or mechanisms of up- or down-stream regulation. Also disease-relevant genes often occur in families of related genes. For example if one member of a kinase family functions as an oncogene, a tumor suppressor, or has been found to be disrupted in an immune,  
15 neurologic, cardiovascular, or metabolic disorder, frequently other family members may play a related role.

The expression analysis organizes kinases into groups that are transcriptionally upregulated in tumors and those that are more restricted to specific tumor types such as melanoma or prostate. This analysis also identifies genes that are regulated in a cell cycle  
20 dependent manner, and are therefore likely to be involved in maintaining cell cycle checkpoints, entry, progression, or exit from mitosis, oversee DNA repair, or are involved in cell proliferation and genome stability. Expression data also can identify genes expressed in endothelial sources or other tissues that suggest a role in angiogenesis, thereby implicating them as targets for control of diseases that have an angiogenic  
25 component, such as cancer, endometriosis, retinopathy and macular degeneration, and various ischemic or vascular pathologies. A proteins' role in cell survival can also be suggested based on restricted expression in cells subjected to external stress such as oxidative damage, hypoxia, drugs such as cisplatinum, or irradiation. Metastases-associated genes can be implicated when expression is restricted to invading regions of a  
30 tumor, or is only seen in local or distant metastases compared to the primary tumor, or when a gene is upregulated during cell culture models of invasion, migration, or motility.



Chromosomal location can identify candidate targets for a tumor amplicon or a tumor-suppressor locus. Summaries of prevalent tumor amplicons are available in the literature, and can identify tumor types to experimentally be confirmed to contain amplified copies of a kinase gene which localizes to an adjacent region.

5 Based on these criteria several kinases immediately stand out as being of potential therapeutic relevance. The protein kinases can be divided into the following disease-relevant categories (nucleotide Seq ID #s in parentheses):

Tumor associated: Mok (SEQ ID NO:57), EPK2, AA316804 (SEQ ID NO:11), AA435956 (SEQ ID NO:48), AA278842 (SEQ ID NO:88), AA599286 (SEQ ID NO:89), AA826850 (SEQ ID NO:3), HRI (SEQ ID NO:73), MLK4 AA232253 (SEQ ID NO:82), AA883975 SGK 235 (SEQ ID NO:95), AA311714 (SEQ ID NO:101), MPSK1 (SEQ ID NO:110), R19609 (Seq ID111), AA383293 (SEQ ID NO:26).

Prostate-specific: AA234451 (SEQ ID NO:47), TSK4 (SEQ ID NO:93), RIP4 (SEQ ID NO:84), KIAA0965 (SEQ ID NO:8).

15 Oncogenic or proliferation associated: KIAA0781 (SEQ ID NO:38), AA789239 (SEQ ID NO:52), CCRK (SEQ ID NO:54), CLK4 (SEQ ID NO:55), H85389 (SEQ ID NO:97).

Neuronal restricted: CAMKKB (SEQ ID NO:66)

Hematopoietic expressed: PTK9L (SEQ ID NO:22), DRAK2 (SEQ ID NO:29), AI025291 (SEQ ID NO:94)

Angiogenic or endothelial expressed: DRAK1 (SEQ ID NO:31), MAK-V (SEQ ID NO:40), TRAD (SEQ ID NO:44), MOK (SEQ ID NO:57), AA08847 (SEQ ID NO:78), HGP\_66444466 (SEQ ID NO:79), RSK4 (SEQ ID NO:16).

25 Cell cycle regulated: AA454060 (SEQ ID NO:45), KIAA0999 (Mitotic – SEQ ID NO:32), AA579641 (Mitotic – SEQ ID NO:60), AA305176 (Mitotic – SEQ ID NO:6), AA018361 (S1 phase – SEQ ID NO:100).

#### VIII. Transgenic Animals.

A variety of methods are available for the production of transgenic animals associated with this invention. DNA can be injected into the pronucleus of a fertilized egg before fusion of the male and female pronuclei, or injected into the nucleus of an embryonic cell (e.g., the nucleus of a two-cell embryo) following the initiation of cell division (Brinster *et al.*, Proc. Nat. Acad. Sci. USA 82: 4438-4442, 1985). Embryos can

be infected with viruses, especially retroviruses, modified to carry inorganic-ion receptor nucleotide sequences of the invention.

Pluripotent stem cells derived from the inner cell mass of the embryo and stabilized in culture can be manipulated in culture to incorporate nucleotide sequences of the invention. A transgenic animal can be produced from such cells through implantation into a blastocyst that is implanted into a foster mother and allowed to come to term. Animals suitable for transgenic experiments can be obtained from standard commercial sources such as Charles River (Wilmington, MA), Taconic (Germantown, NY), Harlan Sprague Dawley (Indianapolis, IN), etc.

The procedures for manipulation of the rodent embryo and for microinjection of DNA into the pronucleus of the zygote are well known to those of ordinary skill in the art (Hogan *et al.*, *supra*). Microinjection procedures for fish, amphibian eggs and birds are detailed in Houdebine and Chourrout (Experientia 47: 897-905, 1991). Other procedures for introduction of DNA into tissues of animals are described in U.S. Patent No., 4,945,050 (Sanford *et al.*, July 30, 1990).

By way of example only, to prepare a transgenic mouse, female mice are induced to superovulate. Females are placed with males, and the mated females are sacrificed by CO<sub>2</sub> asphyxiation or cervical dislocation and embryos are recovered from excised oviducts. Surrounding cumulus cells are removed. Pronuclear embryos are then washed and stored until the time of injection. Randomly cycling adult female mice are paired with vasectomized males. Recipient females are mated at the same time as donor females. Embryos then are transferred surgically. The procedure for generating transgenic rats is similar to that of mice (Hammer *et al.*, Cell 63:1099-1112, 1990).

Methods for the culturing of embryonic stem (ES) cells and the subsequent production of transgenic animals by the introduction of DNA into ES cells using methods such as electroporation, calcium phosphate/DNA precipitation and direct injection also are well known to those of ordinary skill in the art (Teratocarcinomas and Embryonic Stem Cells, A Practical Approach, E.J. Robertson, ed., IRL Press, 1987).

In cases involving random gene integration, a clone containing the sequence(s) of the invention is co-transfected with a gene encoding resistance. Alternatively, the gene encoding neomycin resistance is physically linked to the sequence(s) of the invention.

Transfection and isolation of desired clones are carried out by any one of several methods well known to those of ordinary skill in the art (E.J. Robertson, *supra*).

DNA molecules introduced into ES cells can also be integrated into the chromosome through the process of homologous recombination (Capecchi, Science 244: 1288-1292, 1989). Methods for positive selection of the recombination event (*i.e.*, neo resistance) and dual positive-negative selection (*i.e.*, neo resistance and gancyclovir resistance) and the subsequent identification of the desired clones by PCR have been described by Capecchi, *supra* and Joyner *et al.* (Nature 338: 153-156, 1989), the teachings of which are incorporated herein in their entirety including any drawings. The final phase of the procedure is to inject targeted ES cells into blastocysts and to transfer the blastocysts into pseudopregnant females. The resulting chimeric animals are bred and the offspring are analyzed by Southern blotting to identify individuals that carry the transgene. Procedures for the production of non-rodent mammals and other animals have been discussed by others (Houdebine and Chourrout, *supra*; Pursel *et al.*, Science 244:1281-1288, 1989; and Simms *et al.*, Bio/Technology 6:179-183, 1988).

Thus, the invention provides transgenic, nonhuman mammals containing a transgene encoding a kinase of the invention or a gene effecting the expression of the kinase. Such transgenic nonhuman mammals are particularly useful as an *in vivo* test system for studying the effects of introduction of a kinase, or regulating the expression of a kinase (*i.e.*, through the introduction of additional genes, antisense nucleic acids, or ribozymes).

A "transgenic animal" is an animal having cells that contain DNA which has been artificially inserted into a cell, which DNA becomes part of the genome of the animal which develops from that cell. Preferred transgenic animals are primates, mice, rats, cows, pigs, horses, goats, sheep, dogs and cats. The transgenic DNA may encode human STE20-related kinases. Native expression in an animal may be reduced by providing an amount of anti-sense RNA or DNA effective to reduce expression of the receptor.

#### IX. Gene Therapy

Protein kinases of the invention, or their genetic sequences will also be useful in gene therapy (reviewed in Miller, Nature 357:455-460, 1992). Miller states that advances have resulted in practical approaches to human gene therapy that have demonstrated

positive initial results. The basic science of gene therapy is described in Mulligan (Science 260:926-931, 1993).

In one preferred embodiment, an expression vector containing protein kinase coding sequence is inserted into cells, the cells are grown *in vitro*, and then are infused in large numbers into patients. In another preferred embodiment, a DNA segment containing a promoter of choice (for example a strong promoter) is transferred into cells containing an endogenous gene encoding kinases of the invention in such a manner that the promoter segment enhances expression of the endogenous kinase gene (for example, the promoter segment is transferred to the cell such that it becomes directly linked to the endogenous kinase gene).

The gene therapy may involve the use of an adenovirus containing kinase cDNA targeted to a tumor, systemic kinase increase by implantation of engineered cells, injection with kinase-encoding virus, or injection of naked kinase DNA into appropriate tissues.

Target cell populations may be modified by introducing altered forms of one or more components of the protein complexes in order to modulate the activity of such complexes. For example, by reducing or inhibiting a complex component activity within target cells, an abnormal signal transduction event(s) leading to a condition may be decreased, inhibited, or reversed. Deletion or missense mutants of a component, that retain the ability to interact with other components of the protein complexes but cannot function in signal transduction may be used to inhibit an abnormal, deleterious signal transduction event.

Expression vectors derived from viruses such as retroviruses, vaccinia virus, adenovirus, adeno-associated virus, herpes viruses, several RNA viruses, or bovine papilloma virus, may be used for delivery of nucleotide sequences (*e.g.*, cDNA) encoding recombinant kinase of the invention protein into the targeted cell population (*e.g.*, tumor cells). Methods which are well known to those skilled in the art can be used to construct recombinant viral vectors containing coding sequences (Maniatis *et al.*, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, N.Y., 1989; Ausubel *et al.*, Current Protocols in Molecular Biology, Greene Publishing Associates and Wiley Interscience, N.Y., 1989). Alternatively, recombinant nucleic acid molecules encoding protein sequences can be used as naked DNA or in a reconstituted system *e.g.*, liposomes or other lipid systems for delivery to target cells (*e.g.*, Felgner *et al.*, Nature 337:387-8,

1989). Several other methods for the direct transfer of plasmid DNA into cells exist for use in human gene therapy and involve targeting the DNA to receptors on cells by complexing the plasmid DNA to proteins (Miller, *supra*).

In its simplest form, gene transfer can be performed by simply injecting minute amounts of DNA into the nucleus of a cell, through a process of microinjection (Capecchi, Cell 22:479-88, 1980). Once recombinant genes are introduced into a cell, they can be recognized by the cell's normal mechanisms for transcription and translation, and a gene product will be expressed. Other methods have also been attempted for introducing DNA into larger numbers of cells. These methods include: transfection, wherein DNA is precipitated with  $\text{CaPO}_4$  and taken into cells by pinocytosis (Chen *et al.*, Mol. Cell Biol. 7:2745-52, 1987); electroporation, wherein cells are exposed to large voltage pulses to introduce holes into the membrane (Chu *et al.*, Nucleic Acids Res. 15:1311-26, 1987); lipofection/liposome fusion, wherein DNA is packaged into lipophilic vesicles which fuse with a target cell (Felgner *et al.*, Proc. Natl. Acad. Sci. USA. 84:7413-7417, 1987); and particle bombardment using DNA bound to small projectiles (Yang *et al.*, Proc. Natl. Acad. Sci. 87:9568-9572, 1990). Another method for introducing DNA into cells is to couple the DNA to chemically modified proteins.

It has also been shown that adenovirus proteins are capable of destabilizing endosomes and enhancing the uptake of DNA into cells. The admixture of adenovirus to solutions containing DNA complexes, or the binding of DNA to polylysine covalently attached to adenovirus using protein crosslinking agents substantially improves the uptake and expression of the recombinant gene (Curiel *et al.*, Am. J. Respir. Cell. Mol. Biol., 6:247-52, 1992).

As used herein "gene transfer" means the process of introducing a foreign nucleic acid molecule into a cell. Gene transfer is commonly performed to enable the expression of a particular product encoded by the gene. The product may include a protein, polypeptide, anti-sense DNA or RNA, or enzymatically active RNA. Gene transfer can be performed in cultured cells or by direct administration into animals. Generally gene transfer involves the process of nucleic acid contact with a target cell by non-specific or receptor mediated interactions, uptake of nucleic acid into the cell through the membrane or by endocytosis, and release of nucleic acid into the cytoplasm from the plasma membrane or endosome. Expression may require, in addition, movement of the nucleic

acid into the nucleus of the cell and binding to appropriate nuclear factors for transcription.

As used herein "gene therapy" is a form of gene transfer and is included within the definition of gene transfer as used herein and specifically refers to gene transfer to express a therapeutic product from a cell *in vivo* or *in vitro*. Gene transfer can be performed *ex vivo* on cells which are then transplanted into a patient, or can be performed by direct administration of the nucleic acid or nucleic acid-protein complex into the patient.

In another preferred embodiment, a vector having nucleic acid sequences encoding a protein kinase polypeptide of the invention is provided in which the nucleic acid sequence is expressed only in specific tissue. Methods of achieving tissue-specific gene expression are set forth in International Publication No. WO 93/09236, filed November 3, 1992 and published May 13, 1993.

In all of the preceding vectors set forth above, a further aspect of the invention is that the nucleic acid sequence contained in the vector may include additions, deletions or modifications to some or all of the sequence of the nucleic acid, as defined above.

In another preferred embodiment, a method of gene replacement is set forth. "Gene replacement" as used herein means supplying a nucleic acid sequence which is capable of being expressed *in vivo* in an animal and thereby providing or augmenting the function of an endogenous gene that is missing or defective in the animal.

#### X. Administration of Substances

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures, or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being treated, the particular composition being used, and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be formulated in animal models to achieve a circulating concentration range that initially

takes into account the  $IC_{50}$  as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors, and major organs can be also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan, and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows: 1) the compound is administered to mice (an untreated control mouse should also be used); 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and 3) the samples are analyzed for red and white blood cell counts, blood cell composition, and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, *Journal of American Veterinary Medical Assoc.*, 202:229-249, 1993). Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness, or toxicity. Gross abnormalities in tissue are noted, and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

For the treatment of cancers the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness.

5 Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

### EXAMPLES

10 The examples below are not limiting and are merely representative of various aspects and features of the present invention. The examples below demonstrate the isolation and characterization of the protein kinases of the invention.

#### EXAMPLE 1: Isolation of cDNA clones Encoding Novel Mammalian Protein Kinases 15 Materials and Methods Identification from cDNA databases and isolation of clones encoding novel protein kinases

Novel kinases were identified from the public EST databases using a Hidden Markov model, abbreviated HMM (Krogh, A., Brown, M., Mian, I. S., Sjolander, K., and Haussler, D. 1994. Hidden Markov models in computational biology: Applications to protein modeling. *J. Mol. Biol.*, 235:1501-1531). The model was built with 70 mammalian and yeast kinase catalytic domain sequences. These sequences were chosen from a comprehensive collection of kinases such that no two sequences had more than 50% sequence identity. ESTs were translated in six open reading frames and were searched against the model. ESTs that had a score of at least 10 against the HMM were then masked for repetitive sequences and vectors and were clustered using MSA. The resulting contigs were searched against known kinases to identify EST clones that encode novel kinases.

20 Approximately 40% of the ESTs encoding potentially novel kinases did not correspond to the correct EST upon sequence analysis. Most of these discrepancies were resolved by ordering additional clones, however, 14 remained unavailable. These 14 ESTs were amplified from a variety of single-stranded cDNA sources with primers derived from the corresponding EST entry as shown on Table 5. The PCR product was subcloned into a bluescript vector, digested to confirm the presence of a correct size insert and sequenced. Full sequencing of EST and PCR was carried out using a cycle sequencing Big-dye kit



with AmpliTaq DNA Polymerase, FS (ABI, Foster City, CA). Sequencing reaction products were run on an ABI Prism 377 DNA Sequencer.

Table 5: Primers used to clone PCR products corresponding to novel kinases

	ID#	ID#	Parent	5' primer	3' primer
sp	na	aa	Sequence	Sequence*	Sequence*
H	33	153	2R22-5-11	GAGATCGRNTTYAARGA RTTYGA	TGTCACNCCNAGNSWCCAN AYRTT
M	81	200	5R57_10_2_ m TESK2_m	GCTGCTGGACAGTGACT TGATTTT	GAAAGCAAAGCCTTCACAC CTT
H	67	187	5R69_17_2_h	CTCTCACCTCAGGAAGT GG	GCTTGCGGATCTTCTCA
H	46	166	SGK309_h	GACATCCTGCCGGCCAA CTACG	CGGCCCTGGAGCTGCATCA CTA
M	67	228	5R72_16_2_h	TGCGCGACACCATTGAC CAG	CTCAGGGCTTACATACAGA G
H	45	165	5R72_8_2_h	AAAGGAGAACTACATTT TGAAAAAT	CTTCATCATCTCTAATACAT TGGTTGG
H	41	161	Z36720	CAAATTAAGATCATTGA CTTTGGG	GGAAACAAAGTCCTTGGCC TC
H	115	234	AL031652 - Pak6	GTGGACATCTGGTCCCT CG	GTAGGTCCTTCACTCTTGG AG

- degenerate oligonucleotide residue designation:

5 N= A,C,G or T

R= A or G

Y= C or T

S = C or G

W= A or T

10

#### Full-length sequence extension of protein kinases using cDNA and genomic databases

Extension of partial cDNA sequences to encompass the full-length open-reading frame was carried out by iterative blastn searching of the cDNA databases listed in Table 6. All blastn searches were conducted using a blosum62 matrix, a penalty for a nucleotide mismatch of -3 and reward for a nucleotide match of 1. The gapped blast algorithm is described in: (Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and

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PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402).

Table 6. Databases used for cDNA-based sequence extensions

Database	Database Date
LifeGold templates	Feb 2000
LifeGold compseqs	Feb 2000
LifeGold compseqs	Mar 2000
LifeGold compseqs	Apr 2000
LifeGold fl	Feb 2000
LifeGold flt	Apr 2000
NCBI human Ests	May 2000
NCBI murine Ests	May 2000
NCBI nonredundant	May 2000

5

Extension of partial cDNA sequences to encompass the full-length open-reading frame was also carried out by iterative searches of genomic databases. Three methods were used. The first method made use of the Smith-Waterman algorithm to carry out protein-protein searches of the closest homologue or orthologue to the partial kinase. The target databases consisted of Genescan and open-reading frame (ORF) predictions of all human genomic sequence derived from the human genome project (HGP) as well as from Celera. The complete set of genomic databases searched is shown in Table 7 below. Genomic sequences encoding potential extensions were further assessed by blastp analysis against the NCBI nonredundant to confirm the novelty of the hit. The extending genomic sequences were incorporated into the cDNA sequence after removal of potential introns using the Seqman program from DNASTar. The default parameters used for Smith-Waterman searches were as shown next. Matrix: blosum 62; gap-opening penalty: 12; gap extension penalty: 2. Genescan predictions were made using the Genescan program as detailed in (Chris Burge and Sam Karlin "Prediction of Complete Gene Structures in Human Genomic DNA", JMB (1997) 268(1):78-94). ORF predictions from genomic DNA were made using a standard 6-frame translation.

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The second method for genomic sequence-based extensions made use of tBlastn searches of the homologue or orthologue to the partial kinase against the cDNA databases listed in Table 7. The recognition of significant hits in these databases made possible to identify bridging partial cDNA clones. The iterative application of the two methods made possible the assemblage of the virtual full-length sequence for a large number of the kinases presented in this application. All tblastn searches were conducted using a blosum62 matrix, a penalty for a nucleotide mismatch of -3 and reward for a nucleotide match of 1.

The last method for defining cDNA extensions from genomic sequence used iterative searches of genomic databases through the Genescan program to predict exon splicing and the Genewise program (<http://www.sanger.ac.uk/Software/Wise2/>) to predict potential ORFs based on homology to the closest orthologue/homologue.

Table 7. Databases used for genomic-based sequence extensions

Database	Number of entries	Database Date
Celera v. 1-5	5,306,158	Jan 19/00
Celera v. 6-10	4,209,980	Mar 24/00
Celera v. 11-14	7,222,425	Apr 24/00
Celera v. 15	243,044	May 14/00
HGP all Genescan	25,885	Apr 04/00
HGP; Phase 0	4,944	May 04/00
HGP; Phase 1	28,478	May 05/00
HGP; Phase 2	1,508	May 04/00
HGP; Phase 3	9,971	May 05/00

#### Virtual Extensions

Human AA826850 (SEQ ID NO: 3, SEQ ID NO:124)

Blastn analysis of the partial AA826850 sequence revealed an extension to encompass the complete ORF in the Incyte EST 238299.1. A frame-shift correction at position 595 of this EST (marked by X in NA sequence) generated an uninterrupted ORF.

Human AA960957 (SEQ ID NO: 4, SEQ ID NO:125)

Since the initial filing of this application, the partial AA960957 sequence appeared in the public database as the full-length gene for a protein kinase encoded by a gene that maps adjacent to the *evc* (AJ250839) (ellis-van creveld syndrome and weyers acrodermal dysostosis) gene from 4p16.1.

5 Human 5R79-46-1\_h (SEQ ID NO: 5, SEQ ID NO:126)

Blastn analysis of the partial 5R79-46-1 sequence revealed an extension to encompass the complete ORF in the Incyte EST 463894.6. Since the initial filing of this application, the full-length virtual 5R79-46-1 appeared in the public database as the full-length gene for the TANK-binding kinase (TBK1) (Pomerantz, J.L. and Baltimore, D. (1999) EMBO J. 18 (23), 6694-6704). TBK1 participates in NF- $\kappa$ B activation through the formation of a signaling complex with TRAF2 and TANK.

Human AA305176 (SEQ ID NO: 6, SEQ ID NO:127)

Blastn analysis of the partial AA305176 sequence revealed an extension to encompass the complete ORF in the Incyte EST 220937.1.

15 Human AA256100 (SEQ ID NO: 8, SEQ ID NO:129)

Blastn analysis of the partial AA256100 sequence revealed an extension to encompass the complete ORF through the assembly of three partial clones: Incyte EST 480815.6, KIAA0965 (BAA76809) and AA256100.

Human AA210825 (SEQ ID NO: 9, SEQ ID NO: 130)

20 Blastn analysis of the partial AA210825 sequence revealed an extension to encompass the nearly complete ORF through the assembly of three partial clones: Incyte EST 014721.7, and the NCBI EST's AW01158 and AA210825. An insertion of two "N's" at positions 1915 and 1916 generated an uninterrupted ORF. Blastx analysis indicated the possibility of a start Met in the range of 400-450 nucleotides (i.e. compared to the closest homolog, human PKCmu (CAA53384.1). However, no Met was found in this region; rather ORF ends in an in-frame stop preceded by the sequence  
25 "RGLLAPGDPPCPPNPAPATPPSSRLPTLFSNFCDS". It is possible that part of the sequence covered by nucleotide positions 1-400 derived from AW01158 comes from an intron, explaining the absence of a start Met.

30 Human AA127299 (SEQ ID NO:10, SEQ ID NO:131)

No entries in the database extended this sequence. The 1684 bp insert of this EST contains a 1369 bp intron at the 3' end. Blastx and SW analysis of the 315 bp coding

region revealed homology to the extracatalytic C2 domain of PKC. This EST, may or may not encode a kinase.

Human AA316804 (SEQ ID NO:11, SEQ ID NO:132)

Since the initial filing of this application, the partial AA316804 sequence appeared  
5 in the public database as the full-length gene for the PKC family protein kinase EPK2 or PKC $\epsilon$  (AB015982).

Human H19102 (SEQ ID NO:14, SEQ ID NO:135)

Genewise and Genescan analyses of the partial H19102 sequence revealed an  
extension from the HGP phase 3 contig 3810672 to encompass the complete catalytic  
10 domain of this EST. Blastn analysis against the non-redundant database revealed that this gene is found in the cosmid AC005726 from chromosome 17. H19102 may encode a dual catalytic kinase given the homology to S6 kinase. Analysis of genomic sequence upstream of the 5' end of H19102 revealed a non-kinase gene oriented in the same polarity as  
H19102 suggestive of the start Met for H19102 being close to the 5' end of the H19102  
15 sequence. From this analysis it is deduced that the second catalytic domain of H19102, if present, is most likely located within the 47334-185,215 bp region of the genomic sequence of AC005726.

Human AA476563 (SEQ ID NO:15, SEQ ID NO:136)

Since the initial filing of this application, the partial AA476563 sequence appeared  
20 in the public database as the full-length gene for the protein kinase RPS6KC1 (NM\_012424) (Zhang, H. et al Genomics (1999) 61, 314-318), which is an S6 kinase mapping to 12q12-q13.1.

Human AA626690 (SEQ ID NO:16, SEQ ID NO:137)

Since the initial filing of this application, the partial AA626690 sequence appeared  
25 in the public database as the full-length gene for the protein kinase RPS6KA6 (AF184965) (Yntema, H.G et al (1999) Genomics 62, 332-343), an S6 kinase commonly deleted in patients with complex X-linked (Xq21.1 ) mental retardation.

Human AI215680 (SEQ ID NO: 17, SEQ ID NO:138)

Since the initial filing of this application, the partial AI215680 sequence appeared  
30 in the public database as the full-length gene encoding a hypothetical protein (AAD30182) from the locus AC006530.4 from chromosome 14.

Human AA887783 (SEQ ID NO:21, SEQ ID NO:142)

Blastn analysis of the partial AA887783 sequence revealed an extension to encompass the nearly complete ORF through the assembly of three partial clones: Incyte 415390R6 and the NCBI EST's AA887783 and N94726. Since the initial filing of this application, the nearly full-length virtual AA887783 sequence appeared in the public database as the full-length gene encoding SGK3 (AF169035), a serum- and glucocorticoid-induced protein kinase (Kobayashi, T. et al (1999) Biochemical J. 344, 189-197.

Human R47805 (SEQ ID NO:22, SEQ ID NO:143)

A cDNA clone encoding the full-length ORF of R47805 was isolated using R47805 as a screening probe. A full-length form for R47805 has also appeared in the public database as

PTK9L (NM\_007284), an A6-related protein kinase.

Human H60215 (SEQ ID NO:23, SEQ ID NO:144)

Blastn analysis of the partial H60215 sequence revealed an extension to encompass the complete ORF in the public EST AI275726. This was confirmed through the full insert sequencing of this EST (2,310 bp) which corresponds to the sequence under SEQ ID NO:144.

A different stop codon was predicted for AI275726 compared to H60215 due to a single nucleotide insertion at position 1586 in AI275726. Evidence for the extra nucleotide comes from EST AI191922.

SGK324\_h orthologue of W30246\_m (SEQ ID NO:24, SEQ ID NO:145)

Blastn, blastx and Smith-Waterman analyses of genomic databases revealed an extension to encompass the complete ORF corresponding to the human orthologue of murine W30246. Exons predicted from the following sequences were used for contig construction: Celera 17000189645083, 17000057549105 and 11000501939981; Incyte142404.1, HGP\_7249119, Incyte 7196489H1, Celera 11000501939981, 17000028165594; Incyte 7249119\_3, Celera 17000035772368, 11000502081575 and 17000140274329. The latter Celera sequence provides the N-terminus.

Human AA383293 (SEQ ID NO:26, SEQ ID NO:147)

Blastn, blastx and Smith-Waterman analyses of genomic databases revealed an extension to encompass the complete ORF corresponding for AA383293. Exons predicted from the following sequences were used for contig construction: (numbers in parenthesis

refer to the aa sequence of the closest homolog (RU2S, NP\_057440) used for the Smith-Waterman query): N-term from Incyte 6010175\_2 (14-97), Incyte 6981981 (134-184) 7596749 (186-232) Celera 17000020789545 (243-301) CAB75619.1 (310-341)--(56-145 DCX homology) 6010175\_2 , Celera 17000030058129 (241-262 DCX homology).

5 Human AA021445 (SEQ ID NO:32, SEQ ID NO:152)

Blastn analysis revealed an extension to encompass the nearly complete ORF corresponding for AA021445. Contig reconstruction was as follows: nucleotides 1-802 from KIAA0999 (AB023216); nucleotides 803-4321 from full-insert sequence of AA021445. A pairwise alignment between the AA021445 and KIAA0999 revealed three  
10 inserts in the extracatalytic C-terminus of 48, 48 and 161 aminoacids. In addition, both AA021445 and KIAA0999 have 15 copies of a CAG repeat. Trinucleotide repeats are often found in genes that linked to neurodegenerative diseases.

Human 2R22-55-1 (SEQ ID NO:33, SEQ ID NO:153)

Blastn analysis revealed an extension in the Incyte EST clone 321074.1 to  
15 encompass the complete ORF corresponding to 2R22-55-1.

Human orthologue of AA544838\_m (SEQ ID NO:36, SEQ ID NO:156)

tBlastn analysis identified the partial human KIAA0135 (U79240) clone as the human orthologue of murine AA544838. Blastn revealed an extension KIAA0135\_h (U79240) to encompass the complete ORF. The full ORF was reconstructed from  
20 Incyte406786.5, KFZp430051 and KIAA0135 (U79240).

Human orthologue of A1785735\_m (SEQ ID NO:38, SEQ ID NO:158)

tBlastn analysis identified the partial human KIAA0781 (AB018324) clone as the human orthologue of murine A1785735. Blastn revealed an extension KIAA0135\_h (U79240) to encompass the complete ORF. The full ORF was reconstructed from Incyte  
25 986123.37 KIAA0781 (AB018324).

Human AA207220 (SEQ ID NO: 39, SEQ ID NO:159)

Blastn analysis revealed an extension to encompass the nearly complete ORF corresponding for AA021445. The full ORF was reconstructed from Incyte 402740.1 and AA207220. Frame corrections: deletion of 441 and 595 over Inc402740.1 seq based on  
30 blastx to keep frame open; two n insertions 940, 941 over AA207220 to keep frame open.

Human AA426580 (SEQ ID NO:40, SEQ ID NO:160)

Since the initial filing of this application, the partial AA426580 sequence appeared in the public database as the full-length gene encoding MAK-V (AJ271722) from chromosome 21q22.1.

Human 5R79-54-1 (SEQ ID NO: 41, SEQ ID NO:161)

5 Genewise and Genescan analyses of the partial 5R79-54-1 sequence revealed an extension from genomic sequence to encode the full ORF for 5R79-54-1.

Human orthologue of AA542015\_m (SEQ ID NO: 42, SEQ ID NO:162)

10 tBlastn analysis identified KIAA1297 (AB037718). Blastn extended the KIAA1297 sequence to provide the C-terminus through the Incyte 224074.1 EST. The partial ORF consists of a dual catalytic domain flanked by 6 Ig domains and 2 fibronectin repeats. Based on homology to the bt drosophila protein (AAF59316.1), the human form of AA542015 is expected to be missing 16 Ig domains.

Human R19772 (SEQ ID NO:44, SEQ ID NO:164)

15 The full-length ORF for R19772 was isolated by screening a cDNA library using a probe derived from R19772. Since the initial filing of this application, the R19772 sequence appeared in the public database as the full-length gene encoding Trio (Duet) (AB011422). CDNA library screening revealed multiple isoforms for this gene which are summarized in the Table below.

20 Table 8. Isoforms for R19772

Kestrl Name	Kestrl AA Acc #	Isoform type	Source	Description*
Trad (Duet)	R19772	B	Skeletal muscle	Deletion of K at 124
				Deletion of Q at 616
				Substitution of E for G at 762
		C	Skeletal muscle	Deletion of K at 124
				Deletion of Q at 616
				Substitution of E for G at 762



				Deletion of 32 aa (160-191)
		D	Lung tumor	Deletion of Q at 616
				Deletion of 32 aa (160-191)
		E	Lung tumor	Deletion of Q at 616
				Deletion of 32 aa (160-191)

\* reference amino acid position are with respect to sequence of Trad (AB011422)

Human AA435956 (SEQ ID NO:48, SEQ ID NO:168)

5        Blastn analysis revealed an extension to encompass the nearly complete catalytic region of AA435956. 5' end sequence extension was provided by genomic locus AC007242.3\_h (range 44880-43801). Based on blastx analysis, the extended sequence encodes is full-length at the C-terminus.

Human AA397553 (SEQ ID NO: 51, SEQ ID NO:171)

10       Since the initial filing of this application, the partial AA397553 sequence appeared in the public database as the full-length gene encoding CRK7 (AF227198), a novel CDC2-related protein kinase that colocalizes with interchromatin granule clusters.

Human AA789239 (SEQ ID NO: 52, SEQ ID NO:172)

15       Since the initial filing of this application, the partial AA789239 sequence appeared in the public database as the full-length gene encoding NKIAMRE (AF130372), a novel kinase deleted in human leukemia.

Human AA631990 (SEQ ID NO:55, SEQ ID NO:175)

20       Blastn analysis revealed an extension to encompass the full-length ORF for AA631990. The full ORF was reconstructed from 253847.5 and AA631990 and AA207220. Frame corrections: delete 1 C at 1380, delete 2N's at 2033/2034.

Human AA557536 (SEQ ID NO:56, SEQ ID NO:176)

25       Blastn analysis revealed an extension to encompass full-length ORF for AA557536. The full ORF was reconstructed from AA557536, celera 11000504061899 and the Incyte 097089.1 EST. An 85bp intron was removed from AA557536.

Human N34132 (SEQ ID NO: 63, SEQ ID NO:183)

Full sequencing of EST N34132 (1.3 kb) confirmed that this cDNA encodes a novel NEK-subfamily kinase. Blast analysis against the EST database showed that four

EST sequences (AA283140, AA283140, AA282911 and N53011) extended the sequence of N34132 at the 3' end to form a 2.31 kb contig. Blast analysis of the new contig against the nonredundant public database showed that the N34132 extended contig overlapped (100% identity) over 228 bp at its 3' end with human KIAA0344 (AB002342), a 5,787 bp cDNA encoding a 1246 aa polypeptide. The 5' 790 bp of the KIAA0344 cDNA (encoding the 58 N-terminal protein sequence) were found to be divergent with respect to the extended 2.32 kb N34132 contig. Evidence that the extended N34132 contig (2.31kb) and KIAA0344 (AB002342) belong to the same gene is the following. First, blast analysis of the nucleotide sequences for N34132 and KIAA0344 against the NR database confirmed that these cDNA's are transcribed from the same genomic locus defined by two overlapping BACs (AC004765 and AC004803) from chromosome 12p13.3. Second, full sequence determination of a PCR fragment amplified from single-stranded cDNA confirmed the junction between the extended N34132 contig and KIAA0344\_h (AB002342). The 462 PCR product was amplified with primers CTCCTCAACAGACAGTGCAG (5' primer) and GACATTCTACTACTCGGTCTC (3' primer) designed from the N34132 extended contig and KIAA0344 sequences, respectively. The region of N34132 containing the start Met was isolated by PCR from a testis cDNA library (Clontech).

Human 5R69-17-2 (SEQ ID NO:67, SEQ ID NO:187)

The full-length ORF for 5R69-17-2 was isolated by screening a cDNA library using a probe derived from 5R69-17-2.

Human H85811 (SEQ ID NO:68, SEQ ID NO:188)

Tblastn, Smith-Waterman and blastn analyses using cDNA databases revealed an extension to encompass full-length ORF for H85811. The full ORF was reconstructed from Incyte ESTs 202971.8, 034583.3 and 034583.1 and public ESTs H85811 and AI570599.

Human R43524 (SEQ ID NO:73, SEQ ID NO:192)

Blastn analysis revealed an extension to encompass the complete catalytic region and the C-terminus of R43524. Since the initial filing of this application, the partial R43524 sequence appeared in the public database as the full-length gene encoding the heme-regulated initiation factor 2-alpha kinase (HRI) (AF181071).

Human AA088547 (SEQ ID NO:78, SEQ ID NO:197)

Genewise and Genescan analyses of genomic databases revealed an extension to encompass the complete ORF for AA088547.

Human orthologue of AA139478\_m (SEQ ID NO:80, SEQ ID NO:199)

Tblastn identified the Incyte 211475.1 as the potential full-length human orthologue of murine AA139478

Human AA232253 (SEQ ID NO:82, SEQ ID NO:201)

The full-length ORF for AA232253 was isolated by screening a cDNA library using a probe derived from AA232253. Since the initial filing of this application, the AA232253 sequence appeared in the public database as the full-length gene encoding SLK (AB011422). SLK is a stress-regulated mixed lineage kinase-like protein that activation of Rac and induction of apoptosis. cDNA library screening revealed multiple isoforms for this gene which are summarized in the Table below.

Table 9. Isoforms for AA232253

Kestrl Name	Kestrl AA Acc #	Isoform type	Description*
MLK4	AA232253	MLK4	Substitution of C for W at 346
		MLK4B	Different Cterm (332-800); seq in MLK4B is as shown in *

\* C-terminus specific to MLK4B

LPLAARMSEESYFESKTEESNSAEMSCQITATSNGEHGMNPSLQAMMLMGFGDI  
FSMNKAGAVMHSGMQINMQAKQNSS  
KTTSKRRGKKVNMALGFSDFDLSEGDDDDDDGEEEDNDMDNSE

Human H97685 (SEQ ID NO:84, SEQ ID NO:203)

Blastn analysis revealed an extension to encompass the full-length ORF for H97685. The full ORF was reconstructed from Incyte 474824.1 and the public ESTs H97685 and M62021.

Human A1052250 (SEQ ID NO:87, SEQ ID NO:206)

Blastn analysis revealed an extension to encompass the full-length ORF for AI052250. The full ORF was reconstructed from Incyte 396868.1, the public partial cDNA FLJ10074 (minus intron) and the public ESTs and the public ESTs AI052250 and H97685, AI499220 and M62021.

5 Human AA278842 (SEQ ID NO:88, SEQ ID NO:206)

A nearly full-length cDNA (FL4F12) for AA278842 was isolated by screening a cDNA library using a probe derived from AA278842. A full-length virtual ORF was generated using FL4F12 and AA278842.

Human AA599286 (SEQ ID NO:89, SEQ ID NO:208)

10 Since the initial filing of this application, the partial AA599286 sequence appeared in the public database as a full-length ORF (AK000342).

Human AA425725 (SEQ ID NO:90, SEQ ID NO:209)

15 Since the initial filing of this application, the partial AA425725 sequence appeared in the public database as MSSK1, a serine kinase gene located from human chromosome Xq28.

Human SGK022 orthologue of AA060026\_m (SEQ ID NO:91, SEQ ID NO:210)

Tblastn, Smith-Waterman and blastn analyses of cDNA and genomic databases revealed a potential human orthologue for murine AA060026. The full-length ORF for SGK022 was reconstructed from genomic locus AC022307.

20 Human AA399669 (SEQ ID NO:93, SEQ ID NO:212)

Blastn analysis revealed an extension to encompass the full-length ORF for AA399669. The full ORF was reconstructed as follows: sequence 1-1007 from AL136295.2; sequence 1008-2319 from AA399669 and Incyte 428177.1.

Human AA883975 (SEQ ID NO:95, SEQ ID NO:214)

25 Genescan and Genewise analyses of the genomic databases revealed an extension for AA883975 to encompass the full-length ORF

Human AA905446 (SEQ ID NO:96, SEQ ID NO:215)

30 Tblastn, Smith-Waterman and blastn analyses of cDNA and genomic databases revealed an extension for AA905446 to encompass the full-length ORF. For the Smith-Waterman analysis murine STK22 ( NP\_033462) was used as the closest orthologue. Contig formation: range 162133-163687 from HGP\_h 6921333\_9; removed intron (146-893) predicted from blastx analysis.

Human H29974 (SEQ ID NO: 97 SEQ ID NO:216)

Blastn analysis revealed an extension to encompass a complete catalytic ORF for AA399669. The nearly full-length ORF was reconstructed using Incyte 213829.1 and H29974.

5 Human AA215311 (SEQ ID NO:99, SEQ ID NO:218)

Blastn analysis revealed an extension to encompass the full-length ORF for AA21531. The full ORF was reconstructed from Incyte 067584.1, 022456.1, AA215311 and the reverse complement of CPG\_043208.

Human AA018361 (SEQ ID NO:100, SEQ ID NO:219)

10 The full-length ORF for AA018361 was isolated by screening a cDNA library using a probe derived from AA018361. This yielded clone Sug4-30. Clone Sug4-30, like multiple, independent cDNA clones contained a 181bp intron. The existence of intron-less RNA's was confirmed by a PCR reaction that generated a product that upon sequence analysis skipped the intron region. The full-length virtual ORF for AA018361 was  
15 generated through a contig between AL117482 (seq 1-367) and the sequence for clone Sug4-30.

Human orthologue of AA396601\_m (SEQ ID NO:106, SEQ ID NO:225)

tBlastn and Smith-Waterman analyses of genomic sequence revealed an extension to encompass the full catalytic region for the human orthologue of AA396601. The ORF  
20 was reconstructed from Incyte 018653.9 (7261449H1, 6891740J1) and genomic sequence CPG\_040010.

Human orthologue of AA671275\_m (SEQ ID NO:108, SEQ ID NO:227)

Since the initial filing of this application, a potential human orthologue for murine AA671275 appeared in the public database as the full-length ORF for vaccinia related  
25 kinase 3 (BAA90769).

Human H05721 (SEQ ID NO:111, SEQ ID NO:230)

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for H05721.

Human AI086865 (SEQ ID NO:112, SEQ ID NO:231)

30 Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for AI086865. The full-length ORF was reconstructed from Celera 17000102901516, Incyte 243269.1 and public AL1377531.

Human AA836348 (SEQ ID NO:113, SEQ ID NO:232)

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for AA836348.

Human R86668 (SEQ ID NO:14, SEQ ID NO:233)

5 The full-length ORF for R86668 was isolated by screening a cDNA library using a probe derived from R86668. Since the initial filing of this application, the R8668 sequence appeared in the public database as the full-length gene mitogen-activated protein kinase kinase kinase 6 (MAP3K6) (NM\_00467).

Human 2R41-9-4 (SEQ ID NO: 16, SEQ ID NO:235)

10 The full-length virtual ORF for 2R41-9-4 was generated using genomic sequence to provide the Nterminus for the partial ORF predicted from clone 2R41-9-4

Table 10. Sequences deleted from the provisional patent due to duplication with other genes in the patent

Prov. SEQ ID NO: (na)	Prov. SEQ ID NO: (aa)
160	196
213	214
215	216
122	126
119	123
148	184
4	20
7	23
205	206
14	30
15	31
35	56
42	63
51	72
44	65
77	91

78	92
79	93
80	94
157	193

## Results

Table 1 documents the results from the analysis of the nucleic acid sequence data. From left to right the data presented is as follows. "Gene name" refers to the EST or PCR fragment that defined the novel kinase. "Species" refers to the organism the sequence was derived from. "ID#" refers to the nucleic acid and amino acid sequence ID number designation from this patent. "Kinase family" and "Kinase group" refers to the protein kinase classification defined by sequence homology and based on previously established phylogenetic analysis [Hardie, G. and Hanks S. The Protein Kinase Book, Academic Press (1995) and Hunter T. and Plowman, G. Trends in Biochemical Sciences (1977) 22:18-22 and Plowman G.D. *et al.* (1999) Proc. Natl. Acad. Sci. 96:13603-13610)]. "ORF Start", "ORF End", "ORF Length" refer to the open reading frame range and length as calculated by standard nucleic acid translation programs such as MapDraw (DNASTar). "DNA Repeats" refers to regions of low complexity sequence or repetitive elements such as Alu, LINE, SINE, and LTR sequences. The chromosomal location (CHR localization) for 37 of the 110 novel protein kinases is shown on Table 1 (NA, not available). The methods for determining chromosomal position are outlined below, in Example 2.

Table 2 documents the results from the analysis of the amino acid sequence data. From left to right the data presented is as follows. "Gene name" refers to the EST or PCR fragment that defined the novel kinase. "Species" refers to the organism the sequence was derived from. "ID#" refers to the nucleic acid and amino acid sequence ID number designation from this patent. "Kinase family" and "Kinase group" refers to the protein kinase classification defined by sequence homology and based on previously established phylogenetic analysis [Hardie, G. and Hanks S. The Protein Kinase Book, Academic Press (1995) and Hunter T. and Plowman, G. Trends in Biochemical Sciences (1977) 22:18-22 and Plowman G.D. *et al.* (1999) Proc. Natl. Acad. Sci. 96:13603-13610)]. "nraa Score", "ID match aa", "Identity", "Similar", "nraa Match Acc#", "Description" refer to the data obtained using a Smith-Waterman search of the amino acid sequence against the non-

redundant protein database (Matrix: Pam100; gap open/extension penalties 14/1). "Kinase Domain Start", "Kinase Domain End", "Profile Start" and "Profile End" refer to data obtained using a Hidden-Markov Model to define catalytic range boundaries. The profile has a length of 261 amino acids, corresponding to the complete protein kinase catalytic domain. Proteins in which the profile recognizes a full length catalytic domain have a "Profile Start" of 1 and a "Profile End" of 261. The boundaries of the catalytic domain within the overall protein are noted in the "Kinase Domain Start" and "Kinase Domain End" columns.

10 The following abbreviations were used for kinases:

ASK	Apoptosis signal-regulating kinase
CaMK	Ca <sup>2+</sup> /calmodulin-dependent protein kinase
CCRK	Cell cycle-related kinase
CDK	Cyclin-dependent kinase
CK	Casein kinase
DAPK	Death-associated protein kinase
DM	myotonic dystrophy kinase
Dyrk	dual-specificity-tyrosine phosphorylating-regulated kinase
GAK	Cyclin G-associated kinase
GRK	G-protein coupled receptor
GuC	Guanylate cyclase
HIPK	Homeodomain-interacting protein
IRAK	Interleukin-1 receptor-associated kin
MAPK	Mitogen activated protein kinase
MAST	Micotubule-associated STK
MLCK	Myosin-light chain kinase
MLK	Mixed lineage kinase
NIMA	NimA-related protein kinase
PKA	cAMP-dependent protein kinase
RSK	Ribosomal protein S6 kinase
RTK	Receptor tyrosine kinase



SGK	Serum and glucocorticoid-regulated kinase
STK	serine threonine kinase
ULK	UNC-51-like kinase

The following abbreviations were used for species

H	Human
M	Murine
R	Rat
FV	Fowlpox virus
MT	<i>M. thermoautotrophicum</i>
CE	<i>Caenorhabditis elegans</i>
DM	<i>Drosophila melanogaster</i>
OS	<i>Oryza sativa</i>
SP	<i>Schizosaccharomyces pombe</i>
TP	<i>Tetrahymena pyriformis</i>
PI	<i>Petunia inflata</i>
NC	<i>Neurospora crassa</i>
MSV	<i>Medicago sativa</i>
MSV	Moloney murine sarcoma virus
SA	<i>Squalus acanthias</i>
CS	<i>Cucumis sativus</i>
GM	<i>Glycine max</i>
LL	<i>Lilium longiflorum</i>
TV	<i>Trichomonas vaginalis</i>
MP	<i>Mycoplasma pneumoniae</i>
DD	<i>Dictyostelium discoideum</i>
SC	<i>Saccharomyces cerevisiae</i>
MT	<i>Methanobacterium thermoautotrophicum</i>

### Domain and Motif Identification

A Hidden Markov model (HMM) (Krogh, A., Brown, M., Mian, I. S., Sjolander, K., and Haussler, D. (1994). Hidden Markov models in computational biology: Applications to protein modeling. J. Mol. Biol., 235:1501-1531) was used to identify, both catalytic and extracatalytic domains. Table 4 shows extra-catalytic domains that were identified using the HMM program. Other domains such as coiled-coil and pest motifs were identified as described next.

Potential coiled-coil domains were identified using the COILS program ([www.ch.embnet.org/software/COILS\\_form.html](http://www.ch.embnet.org/software/COILS_form.html)). The matrix used was MTIDK with windows of 14, 21, 28 amino acids. Only regions scoring 0.5 or higher were considered to have potential coiled-coil domain region.

Protein sequences containing potential pest motifs were identified using the program PESTfind ([www.at.embnet.org/embnet/tools/bio/PESTfind/](http://www.at.embnet.org/embnet/tools/bio/PESTfind/)). PEST regions in proteins are by definition sequences that tend to be rich in proline, glutamic or aspartic acid, arginine and histidine; they have been associated with increased protein turnover rates (Rogers S. *et al.* (1986) Science 234, 364-368. The algorithm defines PEST sequences as hydrophilic stretches of amino acids greater than or equal to 12 residues in length. Such regions contain at least one P, one E or D and one S or T. They are flanked by lysine (K), arginine (R) or histidine (H) residues, but positively charged residues are disallowed within the PEST sequence. PESTfind produces a score ranging from about -50 to +50. By definition, a score above zero denotes a possible PEST region; a value greater than +5 defines a high probability that there is a PEST domain.

### **Identification of potential coiled-coil domains and PEST domains in N34132**

Potential coiled-coil domains were identified in N34132 (SEQ ID NO:183) using the COILS program. Only regions scoring 0.5 or higher were considered to have potential coiled-coil domain region. The amino acid positions within N34231 scoring for potential coil-coil regions are shown below.

Table 11 coiled-coil domains predicted for N34132

Coiled-coil Region	Amino acid range	Length (aa)
1	124-147	24
2	437-451	15
3	495-526	32
4	1,723-1,749	27

5 Potential PEST domains were identified in N34132 using PESTfind, a value greater than +5 defines a high probability that there is a PEST domain. The amino acid positions within N34132 scoring for potential PEST regions are shown below.

Table 12 Potential Pest domains identified in N34132

PEST Region	Score	Amino acid range	Amino Acid Length
1	+ 4.91	54-95	42
2	+11.4	537-570	34
3	+31.08	1293-1304	12
4	+10.15	1543-1565	23
5	+ 6.17	1698-1732	35

## 10 EXAMPLE 2. Chromosomal Localization of Novel Mammalian Protein Kinases

### Materials and Methods

Several sources were used to find information about the chromosomal localization of each of the genes described in this patent. First, the accession number for the nucleic acid sequence was used to query the Unigene database. The site containing the Unigene search engine is: <http://www.ncbi.nlm.nih.gov/UniGene/Hs.Home.html>. Information on map position within the Unigene database is imported from several sources, including the Online Mendelian Inheritance in Man (OMIM, <http://www.ncbi.nlm.nih.gov/Omim/searchomim.html>), The Genome Database (<http://gdb.infobiogen.fr/gdb/simpleSearch.html>), and the Whitehead Institute human physical map ([http://carbon.wi.mit.edu:8000/cgi-bin/contig/sts\\_info?database=release](http://carbon.wi.mit.edu:8000/cgi-bin/contig/sts_info?database=release)). For example, searching Unigene with W56561, an EST for a MAK-like kinase, the

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following information is retrieved: Chr.14, D14S65-qTEL. The location of this gene on an “ideogram” of the cytogenetic map of chromosome 14 is also provided, showing that W56561 maps to the bottom of chromosome 14, between 14q31 and 14qTel. If Unigene has not mapped the EST, then the nucleic acid for the gene of interest is used as a query against databases, such as dbsts and htgs (described at [http://www.ncbi.nlm.nih.gov/BLAST/blast\\_databases.html](http://www.ncbi.nlm.nih.gov/BLAST/blast_databases.html)) containing sequences that have been mapped already. The nucleic acid sequence is searched using BLAST-2 at NCBI (<http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast>) and is used to query either dbsts or htgs. In addition to the Whitehead and GDB sites mentioned above, Stanford University maintains a useful site for chromosomal mapping from STS data (<http://www-shgc.stanford.edu/RH/rhserverformnew.html>). Matches in htgs are often resolved immediately because the genomic region hit is annotated in the htgs entry. If an exact match match is found (defined roughly as 99% identity over a region of about 100 base pairs or longer, excluding any repetitive sequence), then the mapped position of the entry in the database is assigned to the original kinase query. Once a cytogenetic region has been identified by one of these approaches, disease association is established by searching OMIM (see above for URL) with the cytogenetic location. OMIM maintains a searchable catalog of cytogenetic map locations organized by disease. A thorough search of available literature for the cytogenetic region is also made using Medline (<http://www.ncbi.nlm.nih.gov/PubMed/medline.html>). References for association of the mapped sites with chromosomal abnormalities found in human cancer can be found in: Knuutila, *et al.*, *Am J Pathol*, 1998, 152:1107-1123.

### Results

The chromosomal location for 37 of the 110 novel protein kinases is shown on Table 1. Three of the novel protein kinases were mapped to regions associated with cancer amplicons, as shown on this table. The regions were also cross-checked with the Mendelian Inheritance in Man database, which tracks genetic information for many human diseases, including cancer. References for association of the mapped sites with chromosomal abnormalities found in human cancer can be found in: Knuutila, *et al.*, *Am J Pathol*, 1998, 152:1107-1123. Association of these mapped regions with other diseases is

documented in the Online Mendelian Inheritance in Man (OMIM)  
(<http://www.ncbi.nlm.nih.gov/htbin-post/Omim>).

### EXAMPLE 3: Generation of Specific Immunoreagents

#### 5 Materials and Methods

Peptide sequences to extra-catalytic regions of novel kinases are chosen which are not homologous to other known kinases based on a Smith Waterman homology search against the non-redundant protein database and predicted to be antigenic based on the DNASTar Protean program. These peptides are conjugated to KLH using Glutaraldehyde.

10 Rabbits are immunized with the KLH-peptide conjugates by four injections three weeks apart. The rabbits are bled ten and fourteen days following the third injection and bled out ten days after the fourth. The serum is checked against the peptide by ELISA.

Table 13. Peptides to be used as immunogens for raising antibodies

Clone Name	SEQ ID NO (aa)	Peptide Sequence	Amino Location
AA8256850	124	KSRDNSRDSSQSEND	339-353
		TECLKRSQDLPRELP	372-386
		RGWRPYDIHS	223-232
5R79-46-1	126	FEGPRRNKEVMYK	224-236
		KDDYNETVHKKTE	451-463
		GTHPKDRNVEKLQ	541-553
		EVSKYQEYTNELQET	643-657
AA256100	129	IDDTSNFDDFPESDI	405-419
		TEPDYKSKDWVFL	427-439
		EEKKLRRSQHARKET	61-75
AA210825	130	SNKDTLRKRHYWRLD	507-521
		RHTTRKSSTTLRE	488-500
		FQNNTTNRYEKEIPL	528-542
		GKHRKTGRDVAVK	668-680
		FPTKQESQLRNE	687-698

AA316804	132	ESHVHQEPSKRIPS	239-252
		HTKRKSSTMVKEGW	409-422
		PSDLDERDEEAVK	375-388
		SPGQGKDHKDLSTSI	543-557
R47805	143	EPVGRWDQDYDRAVL	44-58
		KPKGPGGKRGHKRLI	325-339
		PTDVAQLPSRVPRDA	219-233
AA234451	167	DPFDWEKTGNDGSLT	293-307
		HRPQEKDVWEE	374-385
		RENTDEVFPDEQLSD	340-354
		RSEITQPDRDIPLVR	427-441
AA460132	180	LKSYSTSSKKARPVL	222-236
		KKLDEVRLRGRKRS	237-251
		ETEKTAQGLSNLAKT	131-145
N34132	183	SGRRRRPTKSKGSKS	1848-1862
		PGTAPSKPPLTKAPV	1474-1488
		VSDTQPKAPGIDD	1365-1378
		AHSLDKTSHSSTTGL	1253-1267
5R69-17-2	187	GTTREKTDRVKST	178-190
		HSEAPELHGKIRSSN	138-152
		DETVTPPQFSIV	87-98
		QYDVKSEIYS	204-213
AA278842	206	TVDPEKSVRDQAFKA	515-529
		DSSTADRWDDEDWGS	637-651
		SVSEDPTQLEEEVKD	539-553
AA836348	232	NAPTKRPRSSTVTEA	323-337
		LDSEEDYYTPQKVDV	514-528
		GDKASYRQPKHVEKL	409-423

EXAMPLE 4. Expression analysis of Novel Mammalian Protein KinasesGENE EXPRESSION ANALYSIS

## Tissue Arrays

“cDNA libraries” derived from a variety of sources were immobilized onto nylon  
5 membranes and probed with <sup>32</sup>P-labeled cDNA fragments derived from the gene(s) of interest.

Total RNA or mRNA was used as template in a reverse transcription reaction to generate single-stranded cDNAs (ss cDNA) that were tagged with specific sequences at each end. An oligo dT primer containing a specific sequence (CDS:  
10 AAGCAGTGGTAACAACGCAGAGTACT30VN (V=A,G,C N=A,G,C,T)) anneals at the polyA track at the 3' end of the mRNA and the reverse transcriptase (MMLV RnaseH-) transcribes the antisense strand until it reaches the end of the RNA strand when it adds additional C residues. If a primer (SMII:

AAGCAGTGGTAACAACGCAGAGTACGCGGG or ML2G:

15 AAGTGGCAACAGAGATAACGCGTACGCGGG) ending with 3 Gs is added, it anneals to the added Cs and the MMLV recognizes the rest of the primer sequence as template and continues transcription. As a result, the synthesized cDNAs contain specific sequence tags at both the 5' and the 3' end. When the 5' and the 3' ends are tagged with the same sequence (CDS and SMII) it is referred to as “symmetric.” When the 5' end is tagged  
20 with a different sequence than the 3' end (CDS and ML2G) is referred to as “asymmetric” A double-stranded “cDNA library “ is then generated by PCR amplification using the 3'PCR and ML2 primers (3' PCR: AAGCAGTGGTAACAACGCAGAGT and ML2: AAGTGGCAACAGAGATAACGCGT) that anneal to the added sequence tags.

The amplified “cDNA libraries” were manually arrayed onto nylon membranes  
25 with a 384 pin replicator. The DNA was denatured by alkali treatment, neutralized and cross-linked by UV light. The arrays were pre-hybridized with Express Hyb (Clontech) and hybridized with <sup>32</sup>P labeled probes generated by random hexamer priming of cDNA fragments corresponding to the genes of interest. After washing, the blots were exposed to phosphorimaging cassettes and the intensity of the signal was quantified. The amount of  
30 the DNA on the arrays was also quantified by treating non-denatured or denatured arrays with Syber Green I or Syber Green II respectively (1:100,000 in 50mM Tris, pH8.0) for 2 minutes. After washing with 50mM Tris, pH8.0, the fluorescent emission was detected

with a phosphorimager (Molecular Dynamics) and quantified. The amount of the arrayed DNA was used to normalize the hybridization signal and the corrected values are tabulated in Table 3.

## 5 Results

The results of the microarray expression analysis of the protein kinases presented in this application is shown in Table 3. Data presentation from left to right is as follows: "Tissue": tissue type of the cDNA; "Tumor sym", indicates that the tissue is derived from a tumor, "sym" refers to the fact that the 5' and 3' primers used to make the sample are the same; "Normal Sym", indicates normal tissue was used to make the sample, with symmetric primers as described above; "Tumor 1o", indicates that primary tumor tissue was used to make the cDNA; "Tumor cells", indicates that these cDNA samples were made from cultured tumor cells; "Normal", indicates that these samples are derived from normal tissue or cell lines; "Endos", indicates that these samples are derived from endothelium-related tissue sources; "p53" refers to the status, mutant or wild-type, of the p53 gene in the source samples. Normalized expression values are presented for each gene referred to by its SEQ ID# on the subsequent columns. Genes represented in expression Table 3 are: SEQ ID NO:3 (AA826850), SEQ ID NO:5 (TBK1), SEQ ID NO:6 (AA305176), SEQ ID NO:8 (AA256100), SEQ ID NO:9 (CAB43292), SEQ ID NO:11 (EPK2), SEQ ID NO:12 (PKNbeta), SEQ ID NO:14 (H19102), SEQ ID NO:16 (RSK4), SEQ ID NO:17 (AAD30182), SEQ ID NO:20 (SGK2), SEQ ID NO:22 (PTK9L), SEQ ID NO:26 (AA383293), SEQ ID NO:29 (DRAK2), SEQ ID NO:31 (DRAK1), SEQ ID NO:032 (AA015726), SEQ ID NO:40 (MAK-V), SEQ ID NO:044 (TRAD), SEQ ID NO:044 (TRAD), SEQ ID NO:45 (AA454060), SEQ ID NO:47 (AA234451), SEQ ID NO:48 (AA436054), SEQ ID NO:49 (AA626859), SEQ ID NO:51 (KIAA0904), SEQ ID NO:52 (AA789239), SEQ ID NO:54 (CCRK), SEQ ID NO:55 (CLK4), SEQ ID NO:56 (AA557536), SEQ ID NO:57 (W56561), SEQ ID NO:60 (AA579641), SEQ ID NO:63 (NEK7), SEQ ID NO:66 (CAMKKB), SEQ ID NO:68 (HIPK2), SEQ ID NO:72 (R19609), SEQ ID NO:73 (HRJ), SEQ ID NO:78 (AA088547), SEQ ID NO:79 (AA449542), SEQ ID NO:082a (MLK4), SEQ ID NO:82 (MLK4b), SEQ ID NO:84 (RIP4), SEQ ID NO:88 (AA278842), SEQ ID NO:89 (AA195964), SEQ ID NO:90 (MSSK1), SEQ ID NO:93 (TSK4), SEQ ID NO:94 (AI025291), SEQ ID NO:95



(AA948538), SEQ ID NO:96 (AA905446), SEQ ID NO:97 (H85389), SEQ ID NO:100 (AA018361), SEQ ID NO:101 (AA311714), SEQ ID NO:110 (AA452647), SEQ ID NO:111 (AA310219), SEQ ID NO:112 (A1086865), SEQ ID NO:114 (MEKK6), and SEQ ID NO:116 (SuRTK106).

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EXAMPLE 5. Kinase assays for Erk, JNK1 and p38 MAP kinases

293T cells were transiently transfected with HA- p38 or co-transfected with Flag-tagged wt MLK4A, kinase-dead MLK4A, wild-type MLK4B or kinase-dead MLK4B using Lipofectamine 2000 (Lifetech). Cells were lysed 36 hr post-transfection. Cell lysates normalized to contain equivalent amounts of HA-p38 were immunoprecipitated with anti-HA antibody (Mab HA-11, Babco). Immunoprecipitates were split in two portions, one portion was Western-blotted with anti- HA antibody and the other with a phospho-specific p38 antibody (Promega) to detect activated levels of p38. Activation of Erk1 and Jnk1 was measured similarly. (This example applies to AA232253 (SEQ ID NO:82, SEQ ID NO:201).)

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Results:

In transient assays wild-type MLK4A and MLK4B (but not kinase-inactive MLK4A(K45M) or MLK4B(K45M)) activate Erk, JNK1 and p38 MAP kinases.

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EXAMPLE 6. RAC1 guanine-exchange factor assay

293T cells were transiently transfected with HA-Rac1 or co-transfected with Flag-tagged Duet C, Duet E, Dbl and HA-Tiam-1. Cells were lysed 36 hour post-transfection. Cell lysates normalized to contain equivalent amounts of Rac1 were affinity precipitated with immobilized GST-PBD (p21-binding domain of Pak3). Bound proteins were Western blotted and probed with anti-HA antibody to detect levels of activated Rac1. ((This example applies to R199772 (Trad/Duet)(SEQ ID NO:44, SEQ ID NO:164).)

25

Results:

Duet C and Duet E both act as guanine nucleotide exchange factors on Rac1.

### CONCLUSION

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The molecular complexes and the methods, procedures, treatments, molecules, specific compounds described herein are presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art which are encompassed within the spirit of the invention are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention.

All patents and publications mentioned in the specification are indicative of the levels of those skilled in the art to which the invention pertains.

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed.

In particular, although some formulations described herein have been identified by the excipients added to the formulations, the invention is meant to also cover the final formulation formed by the combination of these excipients. Specifically, the invention includes formulations in which one to all of the added excipients undergo a reaction during formulation and are no longer present in the final formulation, or are present in modified forms.

In addition, where features or aspects of the invention are described in terms of Markush groups, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush

group. For example, if X is described as selected from the group consisting of bromine, chlorine, and iodine, claims for X being bromine and claims for X being bromine and chlorine are fully described.

Other embodiments are within the following claims.

What is claimed is:

CLAIMS

1. An isolated, enriched, or purified nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

2. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises a nucleotide sequence that:

(a) encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) is the complement of the nucleotide sequence of (a);

(c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally occurring kinase polypeptide;

(d) encodes a kinase polypeptide having an amino acid sequence

selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
5 SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
10 SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
15 SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
20 SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
25 SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more,  
but not all, of a domain selected from the group consisting of an N-terminal domain, a  
catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region,  
a spacer region, an insert, and a C-terminal tail;

(e) is the complement of the nucleotide sequence of (d);

(f) encodes a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, wherein said domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail;

(g) is the complement of the nucleotide sequence of (f);

(h) encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID

NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID  
NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID  
NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID  
NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID  
5 NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID  
NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID  
NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID  
NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID  
NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID  
10 NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID  
NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID  
NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID  
NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID  
NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID  
15 NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID  
NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID  
NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID  
NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID  
NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID  
20 NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID  
NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID  
NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID  
NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not  
all, of the domains selected from the group consisting of an N-terminal domain, a catalytic  
25 domain, a C-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure  
region, and a C-terminal tail; or

(i) is the complement of the nucleotide sequence of (h).

3. The nucleic acid molecule of claim 1, further comprising a vector or  
promoter effective to initiate transcription in a host cell.



4. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is isolated, enriched, or purified from a mammal.

5. The nucleic acid molecule of claim 4, wherein said mammal is a human.

6. A nucleic acid probe for the detection of nucleic acid encoding a kinase polypeptide in a sample, wherein said polypeptide is selected from the group consisting of  
5 SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141,  
10 SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166,  
15 SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

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7. The probe of claim 6, wherein said polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

8. A recombinant cell comprising a nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

9. The cell of claim 8, wherein said polypeptide is a fragment of a protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

10. An isolated, enriched, or purified kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, 5 SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, 10 SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, 15 SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, 20 SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, 25 SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

11. The polypeptide of claim 10, wherein said polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

12. The polypeptide of claim 10, wherein said polypeptide comprises:

(a) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ

ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ

ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all of the domains selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail

(c) a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID



NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 wherein said domain is selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

13. The kinase polypeptide of claim 10, wherein said polypeptide is isolated, purified, or enriched from a mammal.

14. The kinase polypeptide of claim 13, wherein said mammal is a human.

15. The kinase polypeptide of claim 10, wherein said polypeptide is a AA144574, AA116841, AA256100, AA305176, AA210825, AA316804, AA980090, N42050, AA476563, AA626690, AA960957, H19102, AA045601, AA107515, AA109508 or AA887783 polypeptide.

16. The kinase polypeptide of claim 10, wherein said polypeptide is a H60215, AA197883, AA297313, W30246, AA172300, AA383293, AA542015, H01248, N23936, W44160, 2R22-5-11, 5R72-18-1, AA021445, AA207220, AA426580, AA544838, W90839, 5R79-54-1, AA839940, R19772 or 5R72-8-2 polypeptide.

17. The kinase polypeptide of claim 10, wherein said polypeptide is a AA234451 polypeptide.

18. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R65-16-1, AA061797, AA065538, AA124976, AA397553, AA435956, AA575635, AA626859, AA789239, A1086865, H17727, H29974, AA557536 or N28606 polypeptide.

19. The kinase polypeptide of claim 10, wherein said polypeptide is a AA631990 or W08549 polypeptide.

20. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R72-16-2, R19927 or R43524 polypeptide.

21. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R57-10-2 polypeptide.

5 22. The kinase polypeptide of claim 10, wherein said polypeptide is a AA232253 polypeptide.

23. The kinase polypeptide of claim 10, wherein said polypeptide is a AA430250, AA836348, R86668 or N34132 polypeptide.

10 24. The kinase polypeptide of claim 10, wherein said polypeptide is a AA098024 or SuRTK106 polypeptide.

25. The kinase polypeptide of claim 10, wherein said polypeptide is a R47805, AA099102, AA589241, H85811, AA013524, AA452647, AA840598, AA088547, AA139478, AA826850, R87679, W65887, H97685, W20810, AA599286, AA425725, AA103218, AA711829, AA060026, AA399669, AA758539, AA883975, AA948538, 15 AA018361, AA215311, AA311714, AA498104, 5R69-17-2, 5R69-23-3, 5R69-26-2, AA118352, AA396601, AA671275, AA278842, AA460132 or H05721 polypeptide.

26. An antibody or antibody fragment having specific binding affinity to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

27. The antibody or antibody fragment of claim 26, wherein said polypeptide comprises:

(a) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ

5 ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ  
ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ  
ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ  
ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ  
ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ  
ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ  
ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ  
ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ  
ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ  
10 ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ  
ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ  
ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ  
ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ  
ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ  
15 ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ  
ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ  
ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ  
ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ  
ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ  
20 ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ  
ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and  
SEQ ID NO:242;

(b) an amino acid sequence selected from the group consisting of SEQ  
ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ  
25 ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ  
ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ  
ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ  
ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ  
ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ  
30 ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ  
ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ  
ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ

ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of the domains selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

(c) a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID

NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID  
NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID  
NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID  
5 NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID  
NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID  
NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID  
NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID  
NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID  
10 NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID  
NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID  
NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID  
NO:241, and SEQ ID NO:242 wherein said domain is selected from the group consisting  
of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a  
proline-rich region, a coiled-coil structure region, and a C-terminal tail.

28. A hybridoma which produces an antibody having specific binding affinity to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

29. A method for identifying a substance that modulates kinase activity comprising:

(a) contacting a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,

SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141,  
 SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146,  
 SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151,  
 SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156,  
 5 SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161,  
 SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166,  
 SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171,  
 SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176,  
 SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181,  
 10 SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
 SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
 SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
 SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
 SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
 15 SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
 SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
 SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
 SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
 SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
 20 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
 SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
 and SEQ ID NO:242 with a test substance;

(b) measuring the activity of said polypeptide; and

(c) determining whether said substance modulates the activity of said  
 25 polypeptide.

30. A method for identifying a substance that modulates kinase activity in a  
 cell comprising:

(a) expressing a kinase polypeptide in a cell, wherein said polypeptide  
 is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID  
 30 NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID  
 NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID  
 NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID



5 NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID  
NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID  
NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID  
NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID  
NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID  
NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID  
NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID  
NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID  
10 NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID  
NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID  
NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID  
NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID  
NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID  
NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID  
15 NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID  
NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID  
NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID  
NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID  
NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID  
20 NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID  
NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

- (b) adding a test substance to said cell; and
- (c) monitoring a change in cell phenotype or the interaction between  
said polypeptide and a natural binding partner.

31. A method for treating a disease or disorder by administering to a patient in need of such treatment a substance that modulates the activity of a kinase selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

32. The method of claim 31, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

33. The method of claim 31, wherein said substance modulates kinase activity *in vitro*.

34. The method of claim 33, wherein said substance is a kinase inhibitor.

35. A method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein said method comprises:

- (a) contacting said sample with a nucleic acid probe which hybridizes  
5 under hybridization assay conditions to a nucleic acid target region of a kinase polypeptide  
selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
10 SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
15 SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
20 SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
25 SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
30 SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, said probe comprising the  
nucleic acid sequence encoding said polypeptide, fragments thereof, or the complements  
of said sequences and fragments; and

(b) detecting the presence or amount of the probe:target region hybrid as an indication of said disease.

36. The method of claim 35, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

37. A method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein said method comprises:

(a) comparing a nucleic acid target region encoding said kinase polypeptide in a sample, wherein said kinase polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ

ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or one or more fragments thereof, with a control nucleic acid target region encoding said kinase polypeptide, or one or more fragments thereof; and

(b) detecting differences in sequence or amount between said target region and said control target region, as an indication of said disease or disorder.

38. The method of claim 37, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

Table 1

SP	Prov	Seq	ID	NA	Prov	Seq	ID	AA	SEQ ID	#	na	SEQ ID	#	3a	Family	Group	Length	NA	Length	AA	ORF	Start	ORF	Length	DNA	Repeats	CHR	Position
M										172					AGC	GRK	2087		888					2084				22g11
M										173					AGC	GRK	376		1358					1134				
M										174					AGC	GRK	376		1358					1134				
M										175					AGC	GRK	376		1358					1134				
M										176					AGC	GRK	376		1358					1134				
M										177					AGC	GRK	376		1358					1134				
M										178					AGC	GRK	376		1358					1134				
M										179					AGC	GRK	376		1358					1134				
M										180					AGC	GRK	376		1358					1134				
M										181					AGC	GRK	376		1358					1134				
M										182					AGC	GRK	376		1358					1134				
M										183					AGC	GRK	376		1358					1134				
M										184					AGC	GRK	376		1358					1134				
M										185					AGC	GRK	376		1358					1134				
M										186					AGC	GRK	376		1358					1134				
M										187					AGC	GRK	376		1358					1134				
M										188					AGC	GRK	376		1358					1134				
M										189					AGC	GRK	376		1358					1134				
M										190					AGC	GRK	376		1358					1134				
M										191					AGC	GRK	376		1358					1134				
M										192					AGC	GRK	376		1358					1134				
M										193					AGC	GRK	376		1358					1134				
M										194					AGC	GRK	376		1358					1134				
M										195					AGC	GRK	376		1358					1134				
M										196					AGC	GRK	376		1358					1134				
M										197					AGC	GRK	376		1358					1134				
M										198					AGC	GRK	376		1358					1134				



Table 2

Patent	Seq	Patent	Seq	Family	Group	nraa	Length	ID	match	%	Identity	%	Similar	nraa	Match	Description	Kinase Domain (s)	Kinase Domain (s)	Profile start	Profile end
SP 108	122	AGC	GRK	GRK	GRK	2.7e-314	888	687	88	100	100	100	100	CAB45657.1	BAR2 [Homo sapiens]	191	453	1	261	
H 1	122	AGC	GRK	GRK	GRK	2.7e-314	888	687	88	100	100	100	100	CAB45657.1	BAR2 [Homo sapiens]	191	453	1	261	
M 2	123	AGC	GRK	GRK	GRK	1.30E-180	378	371	98	99	98	99	99	NP 037029.1	Adrenoreceptor kinase, beta 2 (G-protein-linked receptor kin	3	143	121	261	
H 3	124	AGC	GRK	GRK	GRK	5.80E-108	419	262	71	86	71	86	86	CAB76471.1	Serine/threonine protein kinase [Homo sapiens]	28	286	1	261	
M 4	125	AGC	GRK	GRK	GRK	1.40E-137	414	414	100	100	100	100	100	CAB76471.1	Serine/threonine protein kinase [Homo sapiens]	23	283	1	261	
H 5	126	AGC	GRK	GRK	GRK	0	729	729	100	100	100	100	100	NP 037366.1	TANK-binding kinase 1 [Homo sapiens]	9	304	1	261	
H 6	127	AGC	GRK	GRK	GRK	1.20E-09	328	73	48	66	48	66	66	BAA76817.1	KIAA0973 protein [Homo sapiens]	35	310	242	261	
M 7	128	AGC	GRK	GRK	GRK	1.30E-18	88	42	49	71	49	71	71	AAF55594.1	CG7719 gene product [Drosophila melanogaster]	24	44	242	261	
H 8	128	AGC	GRK	GRK	GRK	6.10E-181	464	463	100	100	100	100	100	BAA76809.1	KIAA0965 protein [Homo sapiens]	90	383	1	261	
H 9	130	AGC	GRK	GRK	GRK	8.80E-180	978	615	67	80	67	80	80	NP 002733.1	Protein kinase C, mu [Homo sapiens]	651	907	256	261	
H 10	131	AGC	GRK	GRK	GRK	1.10E-10	105	42	42	57	42	57	57	P05127	Protein kinase C, beta II type (PKC-BETA-2) [Homo sapiens]	19	24	256	261	
H 11	132	AGC	GRK	GRK	GRK	0	890	890	100	100	100	100	100	NP 005804.1	Protein kinase C, nu [Homo sapiens]	578	832	1	261	
H 12	133	AGC	GRK	GRK	GRK	9.4e-319	889	889	100	100	100	100	100	NP 037487.1	PKNbeta [Homo sapiens]	559	818	126	261	
M 13	134	AGC	GRK	GRK	GRK	1.20E-108	205	204	100	100	100	100	100	IC7083	Protein kinase N beta [Homo sapiens]	1	134	1	261	
H 14	135	AGC	GRK	GRK	GRK	3.80E-12	384	94	38	55	38	55	55	AAC82495.1	Ribosomal protein S6 kinase 3 [Homo sapiens]	81	333	1	261	
H 15	136	AGC	GRK	GRK	GRK	2.80E-257	468	469	100	100	100	100	100	NP 036556.1	Ribosomal protein S6 kinase, 52KD, polypeptide 1 [Homo sapiens]	225	459	1	261	
H 16	137	AGC	GRK	GRK	GRK	7.00E-178	745	745	100	100	100	100	100	NP 055311.1	Ribosomal protein S6 kinase, 90KD, polypeptide 6 [Homo sapiens]	73 & 426	330 & 683	1	261	
H 17	138	AGC	GRK	GRK	GRK	9.80E-222	549	549	100	100	100	100	100	NP 035491.1	Unknown [Homo sapiens]	153	539	1	261	
H 18	139	AGC	GRK	GRK	GRK	9.20E-103	431	430	100	100	100	100	100	NP 035491.1	Unknown [Homo sapiens]	98	355	1	261	
M 19	140	AGC	GRK	GRK	GRK	2.80E-157	430	426	99	88	99	88	88	NP 035491.1	Unknown [Homo sapiens]	98	354	24	261	
M 20	141	AGC	GRK	GRK	GRK	2.00E-76	448	375	349	100	100	100	100	NP 009215.1	Serum/glucocorticoid regulated kinase [Mus musculus]	1	169	1	261	
H 21	142	AGC	GRK	GRK	GRK	4.10E-211	349	349	100	100	100	100	100	NP 009215.1	Serum/glucocorticoid regulated kinase [Mus musculus]	182	369	1	261	
H 22	143	AGC	GRK	GRK	GRK	1.40E-19	440	468	65	77	65	77	77	NP 012757.2	SGK-like protein SGK [Homo sapiens]	10	17	253	261	
H 23	144	AGC	GRK	GRK	GRK	1.50E-165	699	699	100	100	100	100	100	NP 012757.2	SGK-like protein SGK [Homo sapiens]	40	333	1	261	
M 24	145	AGC	GRK	GRK	GRK	1.80E-92	297	199	67	83	67	83	83	NP 004217.1	SGK-like protein SGK [Homo sapiens]	10	17	253	261	
M 25	146	AGC	GRK	GRK	GRK	2.80E-48	708	181	44	73	44	73	73	NP 004217.1	SGK-like protein SGK [Homo sapiens]	40	333	1	261	
H 26	147	AGC	GRK	GRK	GRK	2.80E-31	808	147	55	100	100	100	100	NP 004217.1	SGK-like protein SGK [Homo sapiens]	40	333	1	261	
M 28	148	AGC	GRK	GRK	GRK	3.10E-121	372	372	100	100	100	100	100	NP 004217.1	SGK-like protein SGK [Homo sapiens]	40	333	1	261	
M 29	149	AGC	GRK	GRK	GRK	7.90E-93	372	340	91	95	91	95	95	NP 004751.1	Death-associated protein kinase-related 1	32	293	1	261	
M 30	150	AGC	GRK	GRK	GRK	1.20E-113	414	414	100	100	100	100	100	NP 004751.1	Death-associated protein kinase-related 1	61	321	1	261	
H 31	151	AGC	GRK	GRK	GRK	5.90E-185	1311	1053	80	80	80	80	80	NP 004751.1	Death-associated protein kinase-related 1	8	258	1	261	
H 32	152	AGC	GRK	GRK	GRK	1.20E-45	436	153	51	70	51	70	70	BAA76843.1	KIAA0999 protein [Homo sapiens]	74	325	1	261	
H 33	153	AGC	GRK	GRK	GRK	1.40E-32	436	122	46	65	46	65	65	T22427	Hypothetical protein F49C5.4 - [Caenorhabditis elegans]	56	307	1	261	
H 34	154	AGC	GRK	GRK	GRK	1.30E-184	729	729	100	100	100	100	100	AAC15093.1	Cdc25C associated protein kinase C-TAK1 [Homo sapiens]	59	340	1	261	
M 35	155	AGC	GRK	GRK	GRK	3.50E-126	462	462	100	100	100	100	100	AAC15093.1	Cdc25C associated protein kinase C-TAK1 [Homo sapiens]	59	340	1	261	
H 36	156	AGC	GRK	GRK	GRK	5.10E-59	230	183	79	85	79	85	85	R31237.1, partial CDS [Homo sapiens]	R31237.1, partial CDS [Homo sapiens]	999	1258	1	261	
M 37	157	AGC	GRK	GRK	GRK	3.00E-111	826	636	100	100	100	100	100	KIAA0135 gene, related to pim-1 oncogene, [Homo sapiens]	KIAA0135 gene, related to pim-1 oncogene, [Homo sapiens]	1	158	23	261	
M 38	158	AGC	GRK	GRK	GRK	7.30E-80	629	367	57	69	57	69	69	KIAA0135 gene, related to pim-1 oncogene, [Homo sapiens]	KIAA0135 gene, related to pim-1 oncogene, [Homo sapiens]	20	271	1	261	
H 39	159	AGC	GRK	GRK	GRK	1.40E-244	714	714	100	100	100	100	100	BAA09484.1	KIAA0781 protein [Homo sapiens]	53	304	1	261	
H 40	160	AGC	GRK	GRK	GRK	6.20E-76	874	211	63	80	63	80	80	BAA34501.1	KIAA0537 gene product [Homo sapiens]	53	304	1	261	
H 41	161	AGC	GRK	GRK	GRK	0	2286	2227	100	100	100	100	100	NP 055401.1	KIAA0537 gene product [Homo sapiens]	53	304	1	261	
H 42	162	AGC	GRK	GRK	GRK	7.80E-37	127	67	99	99	99	99	99	NP 055401.1	KIAA0537 gene product [Homo sapiens]	53	304	1	261	
M 43	163	AGC	GRK	GRK	GRK	5.00E-20	514	114	41	63	41	63	63	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 44	164	AGC	GRK	GRK	GRK	3.30E-89	508	181	53	68	53	68	68	BAA92535.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 45	165	AGC	GRK	GRK	GRK	8.80E-98	478	188	138	62	78	62	78	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 46	166	AGC	GRK	GRK	GRK	9.60E-39	268	138	62	78	62	78	78	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 47	167	AGC	GRK	GRK	GRK	7.10E-48	247	146	59	75	59	75	75	NP 004187.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 48	168	AGC	GRK	GRK	GRK	0	1287	1284	100	100	100	100	100	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 49	169	AGC	GRK	GRK	GRK	5.00E-20	514	114	41	63	41	63	63	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 50	170	AGC	GRK	GRK	GRK	3.30E-89	508	181	53	68	53	68	68	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 51	171	AGC	GRK	GRK	GRK	8.80E-98	478	188	138	62	78	62	78	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 52	172	AGC	GRK	GRK	GRK	9.60E-39	268	138	62	78	62	78	78	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 53	173	AGC	GRK	GRK	GRK	7.10E-48	247	146	59	75	59	75	75	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 54	174	AGC	GRK	GRK	GRK	0	1287	1284	100	100	100	100	100	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 55	175	AGC	GRK	GRK	GRK	5.00E-20	514	114	41	63	41	63	63	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 56	176	AGC	GRK	GRK	GRK	3.30E-89	508	181	53	68	53	68	68	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 57	177	AGC	GRK	GRK	GRK	8.80E-98	478	188	138	62	78	62	78	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 58	178	AGC	GRK	GRK	GRK	9.60E-39	268	138	62	78	62	78	78	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 59	179	AGC	GRK	GRK	GRK	7.10E-48	247	146	59	75	59	75	75	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 60	180	AGC	GRK	GRK	GRK	0	1287	1284	100	100	100	100	100	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 61	181	AGC	GRK	GRK	GRK	5.00E-20	514	114	41	63	41	63	63	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 62	182	AGC	GRK	GRK	GRK	3.30E-89	508	181	53	68	53	68	68	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 63	183	AGC	GRK	GRK	GRK	8.80E-98	478	188	138	62	78	62	78	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 64	184	AGC	GRK	GRK	GRK	9.60E-39	268	138	62	78	62	78	78	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 65	185	AGC	GRK	GRK	GRK	7.10E-48	247	146	59	75	59	75	75	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 66	186	AGC	GRK	GRK	GRK	0	1287	1284	100	100	100	100	100	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 67	187	AGC	GRK	GRK	GRK	5.00E-20	514	114	41	63	41	63	63	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	
H 68	188	AGC	GRK	GRK	GRK	3.30E-89	508	181	53	68	53	68	68	NP 008995.1	KIAA1297 protein [Homo sapiens]	570	825	1	261	



Table 2 (cont'd)

M	50	170	CMGC	CDK	2.90E-64	296	193	65	78	NP 004187.1	Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sapiens]	1	240	24	261
M	51	171	CMGC	CDK	1.10E-264	1480	1490	100	100	AAF36401.1	CDC2-related protein kinase 7 [Homo sapiens]	21	1020	1	261
H	52	172	CMGC	CDK	9.20E-101	534	275	82	82	AAF36509.1	NIKAMRE [Homo sapiens]	4	385	1	261
H	53	173	CMGC	CDK	1.40E-128	337	322	92	96	AAF34871.1	NIKATRE alpha [Rattus norvegicus]	1	28	235	261
M	54	174	CMGC	CDK	3.00E-68	211	159	79	84	NP 036251.1	Cell cycle related kinase [Homo sapiens]	177	493	134	261
M	55	175	CMGC	CLK	1.50E-242	499	436	91	93	NP 031740.1	Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sapiens]	13	305	1	261
H	56	176	CMGC	RCK	9.10E-89	544	343	57	64	AAO12719.1	Extracellular signal-regulated kinase 7: ERK7 [Rattus norvegicus]	4	285	1	261
H	57	177	CMGC	RCK	2.30E-189	419	419	100	100	NP 055041.1	Renal tumor antigen [Homo sapiens]	4	284	1	261
H	58	178	CMGC	RCK	1.50E-180	632	632	100	100	AAF37278.1	Intestinal cell kinase [Homo sapiens]	109	364	1	261
H	59	179	CMGC	RCK	1.80E-79	413	198	60	77	P20689	MLCK [Rattus norvegicus]	101	187	65	147
H	60	180	Microbial PK	GR262 sc	2.50E-45	253	102	46	67	AAF50789.1	CG10673 gene product [Drosophila melanogaster]	2	267	1	261
H	61	181	Other	C26C2 ce	2.30E-158	508	258	100	100	CAB70864.1	Hypothetical protein [Homo sapiens]	59	66	235	261
H	62	182	Other	C26C2 ce	1.80E-152	281	243	94	98	CAB70864.1	Hypothetical protein [Homo sapiens]	221	479	1	261
H	63	183	Other	C26C2 ce	6.70E-300	1852	1193	99	99	NP 055636.1	KIAA0344 gene product [Homo sapiens]	73	327	1	261
H	64	184	Other	C26C2 ce	1.10E-254	535	535	100	100	NP 037524.1	Nuclear receptor binding protein [Homo sapiens]	1	170	85	261
H	65	185	Other	C26C2 ce	2.50E-208	378	372	98	100	NP 037524.1	Nuclear receptor binding protein [Homo sapiens]	165	446	1	261
H	66	186	Other	C26C2 ce	3.80E-148	588	588	100	100	AAO31507.1	Cg2/rcalmodulin-dependent protein kinase beta [Homo sapiens]	24	285	1	261
H	67	187	Other	CTRI	9.90E-24	287	87	33	52	JO1743	Hypothetical 33.6K protein - rabbit fibroblast virus	199	527	1	261
H	68	188	Other	DYRK	0	1171	1137	97	99	AAD52566.1	Nuclear body associated kinase 1a [Mus musculus]	174	487	1	261
H	69	189	Other	DYRK	2.10E-280	553	553	100	100	NP 003573.1	Dual-specific tyrosine-(Y)-phosphorylation regulated kinase 3	76	103	235	261
M	70	190	Other	DYRK	2.30E-95	168	149	80	96	NP 003573.1	Dual-specific tyrosine-(Y)-phosphorylation regulated kinase 3	167	583	1	261
M	71	191	Other	EIFK	0	1649	1493	90	96	NP 038747.1	GCN2 eIF2alpha kinase [Mus musculus]	101	187	85	147
H	72	192	Other	EIFK	1.50E-220	630	630	100	100	NP 055228.1	Heme-regulated initiation factor 2-alpha kinase [Homo sapiens]	116	150	118	147
H	73	193	Other	Endop	2.50E-45	253	102	46	67	AAF50799.1	CG10873 gene product [Drosophila melanogaster]	165	443	1	261
M	74	194	Other	Endop	3.70E-45	216	100	45	64	AAF50799.1	CG10873 gene product [Drosophila melanogaster]	1	239	19	261
M	75	195	Other	IRAK	0	596	596	100	100	NP 009130.1	Interleukin-1 receptor-associated kinase M [Homo sapiens]	516	777	1	261
M	76	196	Other	IRAK	1.20E-170	352	293	75	85	NP 009130.1	Interleukin-1 receptor-associated kinase M [Homo sapiens]	32	318	1	261
H	77	197	Other	IRE	1.5E-323	922	746	82	89	NP 036146.1	Irf1, inositol-requiring 1 gene [Mus musculus]	12	266	1	261
H	78	198	Other	KYK2 dd	8.70E-40	225	102	45	82	AAF48758.1	CG8173 gene product [Drosophila melanogaster]	12	39	101	128
H	79	199	Other	KYK2 dd	5.90E-32	280	109	32	50	AAF48758.1	CG8173 gene product [Drosophila melanogaster]	16	259	1	261
M	80	200	Other	LIMK	2.60E-17	41	37	92	95	NP 009101.1	testis-specific kinase 2 [Homo sapiens]	463	723	1	261
M	81	201	Other	MLK	2.50E-282	800	799	100	100	AAF63490.1	Mixed lineage kinase [Homo sapiens]	357	620	1	261
H	82	202	Other	MLK	8.80E-251	835	835	100	100	AAD29632.1	Putative protein-tyrosine kinase [Homo sapiens]	7	27	181	202
H	83	203	Other	RIP	2.20E-158	634	365	100	100	BAA32317.1	Receptor interacting protein 3 [Mus musculus]	57	83	50	78
H	84	204	Other	RIP	5.30E-158	289	288	100	100	AAF03133.1	Receptor interacting protein 3 [Mus musculus]	32	327	1	261
M	85	205	Other	SCY1 sc	0	688	688	100	100	CAB55300.1	Hypothetical protein [Homo sapiens]	65	131	47	116
H	86	206	Other	SCY1 sc	1.70E-209	505	354	98	98	BAA92598.1	KIAA1360 protein [Homo sapiens]	230	305	81	143
H	87	207	Other	SCY1 sc	2.20E-157	808	396	45	61	AAF56933.1	CG1873 gene product [Drosophila melanogaster]	79	531	1	261
H	88	208	Other	SLOB7	7.40E-196	649	648	100	100	BAA91097.1	Unnamed protein product [Homo sapiens]	10	265	1	261
H	89	209	Other	SRPK	5.80E-252	533	533	100	100	NP 055185.1	Serine/threonine kinase 22A (spmiogenesis associated) [Mus musculus]	25	280	1	261
H	90	210	Other	SRPK	3.80E-53	268	122	46	70	NP 033462.1	Serine/threonine kinase 22B (spmiogenesis associated) [Mus musculus]	12	272	1	261
H	91	211	Other	STK22A	2.70E-52	268	127	48	68	NP 033462.1	Serine/threonine kinase 22B (spmiogenesis associated) [Mus musculus]	12	267	7	261
M	92	212	Other	STK22A	4.80E-16	292	112	45	64	NP 033462.1	Serine/threonine kinase 22B (spmiogenesis associated) [Mus musculus]	1	213	1	261
H	93	213	Other	STK22A	5.10E-123	358	322	90	96	NP 033462.1	Serine/threonine kinase 22B (spmiogenesis associated) [Mus musculus]	80	408	1	261
H	94	214	Other	TSK	2.10E-33	273	122	46	62	NP 033462.1	Serine/threonine kinase 22B (spmiogenesis associated) [Mus musculus]	1	329	1	261
H	95	215	Other	TSK	2.50E-32	216	93	41	58	NP 033462.1	Serine/threonine kinase 22B (spmiogenesis associated) [Mus musculus]	80	408	1	261
H	96	216	Other	UNC	0.000062	333	57	36	56	AAO32787.1	Putative protein kinase [Arabidopsis thaliana]	6	340	1	261
H	97	217	Other	UNC	0.002482	412	53	37	52	BAA77341.1	UNC-51-like kinase (ULK) 2 [Mus musculus]	57	313	1	261
M	98	218	Other	UNC	0.002482	412	53	37	52	BAA77341.1	UNC-51-like kinase (ULK) 2 [Mus musculus]	57	313	1	261
H	99	219	Other	UNC	0.001096	341	50	36	56	BAA77341.1	UNC-51-like kinase (ULK) 2 [Mus musculus]	57	313	1	261
H	100	220	Other	UNC	1.90E-68	480	247	100	100	117265	Hypothetical protein DKFZP434C131.1 - human (fragment)	4	265	1	261
H	101	221	Other	UNC	1.60E-208	565	468	96	96	BAA91270.1	Unnamed protein product [Homo sapiens]	1	39	84	124
H	102	221	Other	UNC	6.70E-10	39	27	69	90	AAO00575.1	Serum-inducible kinase [Homo sapiens]	1	39	84	124

Table 2 (cont'd)

M 103	222	Other	Unique	0.000022	349	38	30	50	CAA18116.1	Serine/threonine protein kinase like protein [Arabidopsis thaliana]	80	159	1	88
H 104	223	Other	Unique	0.000128	704	54	30	45	BAA86578.1	KIAA1284 protein [Homo sapiens]	1	248	25	281
M 105	224	Other	Unique	0.007385	540	25	42	61	AAF47916.1	Tie gene product [Drosophila melanogaster]	9	104	168	281
M 106	225	Other	Unique	0.31334	540	52	30	42	P10182	SALIVARY PROLINE-RICH PROTEIN PO (ALLELE K) [Homo sapiens]	1	272	18	73
H 107	226	Other	Unique	0.022948	365	25	34	57	NP_006276.1	testis-specific kinase 1 [Homo sapiens]	68	96	42	71
M 108	227	Other	VRK	3.10E-263	474	474	100	100	BAA00769.1	Vaccinia related kinase 3 [Homo sapiens]	247	318	63	136
H 109	228	Other	VRK	1.20E-111	234	191	82	90	BAA00769.1	Vaccinia related kinase 3 [Homo sapiens]	7	78	63	136
M 110	229	Other	YPL238 sc	7.40E-144	305	304	100	100	AAC28337.1	MPK [Homo sapiens]	20	290	1	261
H 111	230	Other	YQ09 ce	5.10E-49	581	135	43	63	AAF46188.1	CG4523 gene product [Drosophila melanogaster]	158	507	1	261
H 112	231	STE	NEK	3.30E-30	698	122	48	86	P51954	NEK1 (NIMA-RELATED PROTEIN KINASE 1) [Mus musculus]	4	251	1	261
H 113	232	STE	NEK	2.70E-119	838	357	86	86	AA031939.1	mitogen-activated protein kinase kinase kinase 6 [Homo sapiens]	378	629	6	261
H 114	233	STE	STE11	1.10E-291	719	1011	100	100	NP_004663.1	mitogen-activated protein kinase kinase kinase 6 [Homo sapiens]	449	700	1	261
H 115	234	STE	STE20-02	7.70E-177	719	719	100	100	BAA94194.1	(U40827) protein tyrosine kinase [Mus musculus]	187	453	1	261
H 116	235	TK	RTK-20	4.90E-24	495	77	38	56	AAA08465.1	fibroblast growth factor receptor 3 [Mus musculus]	8	143	123	261
H 117	236	TK	RTK-20	5.30E-18	183	53	39	57	NP_032036.1	fibroblast growth factor receptor 3 [Mus musculus]	35	282	1	261
M 118	237	AGC	SGK	6.30E-112	367	367	100	100	AAF12757.2	Cell cycle related kinase [Homo sapiens]	4	287	1	261
H 120	238	CMGC	CDK	2.80E-137	452	452	100	100	NP_036251.1	Testis-specific kinase 2 [Homo sapiens]	62	293	5	281
H 121	239	Other	LIMK	6.50E-233	555	555	100	100	NP_009101.1	Testis-specific kinase 2 [Homo sapiens]	62	293	5	281

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Table 3





167  
Table 3 (cont'd)[illegible]



[illegible]

Table 3 (cont'd)

Tissue	Tumour - ym	Normal - ym	Tumour - fo	Tumour - dets	Normal - E index	p53	SFG 844	TGRO 45	AN350 41	AN350 44	AA350 43	AN350 31	MUSO 32	AA350 34	EQ350 35	CL
DuPang-1							853031	578	729	0	0	0	0	0	0	0
DuPang-2							24026	264	374	0	0	0	0	0	0	0
DuPang-3							44323	716	150	0	0	0	0	0	0	0
DuPang-4							24067	0	0281	0	0	0	0	0	0	0
DuPang-11							05163	0	4291	0	0	0	0	0	0	0
DuPang-12							201155	284	2111	0	0	0	0	0	0	0
DuPang-10							7804	964	73	0	0	0	0	0	0	0
DuPang-1							3139	231	38	0	0	0	0	0	0	0
DuPang-2							804	1703	265	0	0	0	0	0	0	0
DuPang-3							20551	324	0	0	0	0	0	0	0	0
DuPang-4							40505	0	51	0	0	0	0	0	0	0
DuPang-5							33000	20	0	0	0	0	0	0	0	0
DuPang-6							1954	23	90	0	0	0	0	0	0	0
SV40 - 8	wt						954	212	0	0	0	0	0	0	0	0
SV40 - 8	mutant						0	222	0	0	0	0	0	0	0	0
HCT-116 - 7	wt						771	122	55	0	0	0	0	0	0	0
HCT-116 - 8	mutant						310	0	144	0	0	0	0	0	0	0
HT29 - 1	wt						0	0	23	0	0	0	0	0	0	0
HT29 - 7	mutant						0	0	51	0	0	0	0	0	0	0
HT29 - 8	wt						1307	517	34	0	0	0	0	0	0	0
SF539 - 7	wt						3320	71	130	0	0	0	0	0	0	0
SF539 - 8	mutant						17076	802	0	0	0	0	0	0	0	0
SF-268-7	mutant						15323	20	115	0	0	0	0	0	0	0
SF-268-8	wt						12333	29	0	0	0	0	0	0	0	0
OVCAR-4 - 7	wt						12784	4	175	0	0	0	0	0	0	0
OVCAR-4 - 8	mutant						4732	0	0	0	0	0	0	0	0	0
OVCAR-5 - 7	wt						3130	0	4	0	0	0	0	0	0	0
OVCAR-5 - 8	mutant						3275	440	0	0	0	0	0	0	0	0
MCF-7 - 8	wt						838	0	0	0	0	0	0	0	0	0
ADR-RES - 8	mutant						1097	88	0	0	0	0	0	0	0	0
HsA - 6	wt						1922	217	21	0	0	0	0	0	0	0
SW480 - 7	mutant						412	4	72	0	0	0	0	0	0	0
SW480 - 8	wt						162	10	0	0	0	0	0	0	0	0
H1299 - 8	mutant						0	235	4	0	0	0	0	0	0	0
C33A - 7	wt						444	0	0	0	0	0	0	0	0	0
C33A - 8	mutant						28058	148	84	0	0	0	0	0	0	0
U2OS - 7	wt						4758	418	0							



170  
Table 3 (cont'd)[illegible]

Table 3<sup>171</sup> (cont'd)[illegible]

172  
Table 3 (cont'd)[illegible]

Table 3 (cont'd)

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174  
Table 3 (cont'd)[illegible]

Table 3 (cont'd)

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178.  
Table 3 (cont'd)

Team	Team-yr	Norm-yr	Turn-1	Turn-2	Turn-3	Turn-4	Turn-5	Turn-6	Turn-7	Turn-8	Turn-9	Turn-10	Turn-11	Turn-12	Turn-13	Turn-14	Turn-15	Turn-16	Turn-17	Turn-18	Turn-19	Turn-20	Turn-21	Turn-22	Turn-23	Turn-24	Turn-25	Turn-26	Turn-27	Turn-28	Turn-29	Turn-30	Turn-31	Turn-32	Turn-33	Turn-34	Turn-35	Turn-36	Turn-37	Turn-38	Turn-39	Turn-40	Turn-41	Turn-42	Turn-43	Turn-44	Turn-45	Turn-46	Turn-47	Turn-48	Turn-49	Turn-50	Turn-51	Turn-52	Turn-53	Turn-54	Turn-55	Turn-56	Turn-57	Turn-58	Turn-59	Turn-60	Turn-61	Turn-62	Turn-63	Turn-64	Turn-65	Turn-66	Turn-67	Turn-68	Turn-69	Turn-70	Turn-71	Turn-72	Turn-73	Turn-74	Turn-75	Turn-76	Turn-77	Turn-78	Turn-79	Turn-80	Turn-81	Turn-82	Turn-83	Turn-84	Turn-85	Turn-86	Turn-87	Turn-88	Turn-89	Turn-90	Turn-91	Turn-92	Turn-93	Turn-94	Turn-95	Turn-96	Turn-97	Turn-98	Turn-99	Turn-100	Turn-101	Turn-102	Turn-103	Turn-104	Turn-105	Turn-106	Turn-107	Turn-108	Turn-109	Turn-110	Turn-111	Turn-112	Turn-113	Turn-114	Turn-115	Turn-116	Turn-117	Turn-118	Turn-119	Turn-120	Turn-121	Turn-122	Turn-123	Turn-124	Turn-125	Turn-126	Turn-127	Turn-128	Turn-129	Turn-130	Turn-131	Turn-132	Turn-133	Turn-134	Turn-135	Turn-136	Turn-137	Turn-138	Turn-139	Turn-140	Turn-141	Turn-142	Turn-143	Turn-144	Turn-145	Turn-146	Turn-147	Turn-148	Turn-149	Turn-150	Turn-151	Turn-152	Turn-153	Turn-154	Turn-155	Turn-156	Turn-157	Turn-158	Turn-159	Turn-160	Turn-161	Turn-162	Turn-163	Turn-164	Turn-165	Turn-166	Turn-167	Turn-168	Turn-169	Turn-170	Turn-171	Turn-172	Turn-173	Turn-174	Turn-175	Turn-176	Turn-177	Turn-178	Turn-179	Turn-180	Turn-181	Turn-182	Turn-183	Turn-184	Turn-185	Turn-186	Turn-187	Turn-188	Turn-189	Turn-190	Turn-191	Turn-192	Turn-193	Turn-194	Turn-195	Turn-196	Turn-197	Turn-198	Turn-199	Turn-200	Turn-201	Turn-202	Turn-203	Turn-204	Turn-205	Turn-206	Turn-207	Turn-208	Turn-209	Turn-210	Turn-211	Turn-212	Turn-213	Turn-214	Turn-215	Turn-216	Turn-217	Turn-218	Turn-219	Turn-220	Turn-221	Turn-222	Turn-223	Turn-224	Turn-225	Turn-226	Turn-227	Turn-228	Turn-229	Turn-230	Turn-231	Turn-232	Turn-233	Turn-234	Turn-235	Turn-236	Turn-237	Turn-238	Turn-239	Turn-240	Turn-241	Turn-242	Turn-243	Turn-244	Turn-245	Turn-246	Turn-247	Turn-248	Turn-249	Turn-250	Turn-251	Turn-252	Turn-253	Turn-254	Turn-255	Turn-256	Turn-257	Turn-258	Turn-259	Turn-260	Turn-261	Turn-262	Turn-263	Turn-264	Turn-265	Turn-266	Turn-267	Turn-268	Turn-269	Turn-270	Turn-271	Turn-272	Turn-273	Turn-274	Turn-275	Turn-276	Turn-277	Turn-278	Turn-279	Turn-280	Turn-281	Turn-282	Turn-283	Turn-284	Turn-285	Turn-286	Turn-287	Turn-288	Turn-289	Turn-290	Turn-291	Turn-292	Turn-293	Turn-294	Turn-295	Turn-296	Turn-297	Turn-298	Turn-299	Turn-300	Turn-301	Turn-302	Turn-303	Turn-304	Turn-305	Turn-306	Turn-307	Turn-308	Turn-309	Turn-310	Turn-311	Turn-312	Turn-313	Turn-314	Turn-315	Turn-316	Turn-317	Turn-318	Turn-319	Turn-320	Turn-321	Turn-322	Turn-323	Turn-324	Turn-325	Turn-326	Turn-327	Turn-328	Turn-329	Turn-330	Turn-331	Turn-332	Turn-333	Turn-334	Turn-335	Turn-336	Turn-337	Turn-338	Turn-339	Turn-340	Turn-341	Turn-342	Turn-343	Turn-344	Turn-345	Turn-346	Turn-347	Turn-348	Turn-349	Turn-350	Turn-351	Turn-352	Turn-353	Turn-354	Turn-355	Turn-356	Turn-357	Turn-358	Turn-359	Turn-360	Turn-361	Turn-362	Turn-363	Turn-364	Turn-365	Turn-366	Turn-367	Turn-368	Turn-369	Turn-370	Turn-371	Turn-372	Turn-373	Turn-374	Turn-375	Turn-376	Turn-377	Turn-378	Turn-379	Turn-380	Turn-381	Turn-382	Turn-383	Turn-384	Turn-385	Turn-386	Turn-387	Turn-388	Turn-389	Turn-390	Turn-391	Turn-392	Turn-393	Turn-394	Turn-395	Turn-396	Turn-397	Turn-398	Turn-399	Turn-400	Turn-401	Turn-402	Turn-403	Turn-404	Turn-405	Turn-406	Turn-407	Turn-408	Turn-409	Turn-410	Turn-411	Turn-412	Turn-413	Turn-414	Turn-415	Turn-416	Turn-417
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180  
Table 3 (cont'd)

Item	Material	Unit	Quantity	Price	Amount	Remarks
1	100	100	100	100	100	
2	100	100	100	100	100	
3	100	100	100	100	100	
4	100	100	100	100	100	
5	100	100	100	100	100	
6	100	100	100	100	100	
7	100	100	100	100	100	
8	100	100	100	100	100	
9	100	100	100	100	100	
10	100	100	100	100	100	
11	100	100	100	100	100	
12	100	100	100	100	100	
13	100	100	100	100	100	
14	100	100	100	100	100	
15	100	100	100	100	100	
16	100	100	100	100	100	
17	100	100	100	100	100	
18	100	100	100	100	100	
19	100	100	100	100	100	
20	100	100	100	100	100	
21	100	100	100	100	100	
22	100	100	100	100	100	
23	100	100	100	100	100	
24	100	100	100	100	100	
25	100	100	100	100	100	
26	100	100	100	100	100	
27	100	100	100	100	100	
28	100	100	100	100	100	
29	100	100	100	100	100	
30	100	100	100	100	100	
31	100	100	100	100	100	
32	100	100	100	100	100	
33	100	100	100	100	100	
34	100	100	100	100	100	
35	100	100	100	100	100	
36	100	100	100	100	100	
37	100	100	100	100	100	
38	100	100	100	100	100	
39	100	100	100	100	100	
40	100	100	100	100	100	
41	100	100	100	100	100	
42	100	100	100	100	100	
43	100	100	100	100	100	
44	100	100	100	100	100	
45	100	100	100	100	100	
46	100	100	100	100	100	
47	100	100	100	100	100	
48	100	100	100	100	100	
49	100	100	100	100	100	
50	100	100	100	100	100	
51	100	100	100	100	100	
52	100	100	100	100	100	
53	100	100	100	100	100	
54	100	100	100	100	100	
55	100	100	100	100	100	
56	100	100	100	100	100	
57	100	100	100	100	100	
58	100	100	100	100	100	
59	100	100	100	100	100	
60	100	100	100	100	100	
61	100	100	100	100	100	
62	100	100	100	100	100	
63	100	100	100	100	100	
64	100	100	100	100	100	
65	100	100	100	100	100	
66	100	100	100	100	100	
67	100	100	100	100	100	
68	100	100	100	100	100	
69	100	100	100	100	100	
70	100	100	100	100	100	
71	100	100	100	100	100	
72	100	100	100	100	100	
73	100	100	100	100	100	
74	100	100	100	100	100	
75	100	100	100	100	100	
76	100	100	100	100	100	
77	100	100	100	100	100	
78	100	100	100	100	100	
79	100	100	100	100	100	
80	100	100	100	100	100	
81	100	100	100	100	100	
82	100	100	100	100	100	
83	100	100	100	100	100	
84	100	100	100	100	100	
85	100	100	100	100	100	
86	100	100	100	100	100	
87	100	100	100	100	100	
88	100	100	100	100	100	
89	100	100	100	100	100	
90	100	100	100	100	100	
91	100	100	100	100	100	
92	100	100	100	100	100	
93	100	100	100	100	100	
94	100	100	100	100	100	
95	100	100	100	100	100	
96	100	100	100	100	100	
97	100	100	100	100	100	
98	100	100	100	100	100	
99	100	100	100	100	100	
100	100	100	100	100	100	

[illegible]

[illegible]

Table 3 (cont'd)

Tissue	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000
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184  
Table 3 (cont'd)

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Table 187  
(cont'd)

Tissue	Tempor-lym	Neuro-lym	Tumor - ly	Tumor cells	Normal	2 nodes	53	REQ 116
testis								84
adrenal gland - h		2						834
adipose tissue - h		3						822
bone marrow - h		4						2601
musculary gland - h		5						225
brain - h		6						686
pancreas - h		7						2327
cardiac muscle - h		8						2719
pulmonary gland - h		9						1303
testis - h		10						717
prostate - h		11						762
testis - h		12						627
prostate - h		13						848
testis - h		14						410
testis - h		15						0
testis - h		16						184
muscular muscle - h		17						614
heart - h		18						292
small intestine - h		19						250
kidney - h		20						51
spinal cord - h		21						187
bone - h		22						458
liver - h		23						884
stomach - h		24						60
heart - h		25						141
thyroid - h		26						322
thymus - h		27				28		0
HPAEC		28						166
thyroid gland - h		29				30		2128
HPAEC		30						91
trachea - h		31						198
trachea - h		32						180
trachea - h		33						0
trachea - h		34						179
trachea - h		35						71
trachea - h		36						1026
lymph node - h		37						102
muscular muscle - h		38						145
heart - h		39						123
heart - h		40						571
thyroid - h		41						140
Quadratus - h		42						0
testis - h		43						0
Salivary gland - h		44						0
testis - h					303			0
HT1318-normal					303			0
HT1318-normal					261			1292
HT1318-normal					256	256		1227
HT1318-normal					264	254		85
Brain 13					344			0
Brain 17					342			0
cardiac muscle - h					334	334		139
lymph node - h					332			141
HPAEC					330			70
lymph node - h					328			80
lymph node - h					327			386
testis - h					326			0
HPAEC					321			0
thyroid - h					320			148
HT1409 - normal					318			203
HEP-2 cell untreated					318			172
liver - h					314			0
trachea - h					311			86
thyroid gland - h					309			190
salivary gland - h					307			0
prostate - h					305			0
pulmonary gland - h					302			307
pancreas - h					302			16
musculary gland - h					298			80
muscle - h					297			111
testis - h					296			0
bone - h					294			0
liver - h					293			0
spinal cord - h					290			267
small intestine - h					279			126
muscular muscle - h					277			0
bone marrow - h					275	275		0
adipose tissue - h					268			59
HPAEC					268			311
HT302-normal					239	239		222
HT302-normal					222	225		0
Brain 15					224			356
Brain 16					223	223		467
HT327-normal					221	221		87
Brain 7					229	229		442
Brain 8					227	227		80
Brain 9					222			0
Brain 1					215			1006
testis - h					214			0
Heart 1 - h					212			123
stomach - h					212			0
testis - h					211	211		0
prostate - h					210			0
HPAEC					209			267
testis - h					205			0
Quadratus - h					203			0
muscular muscle - h					201			0
pancreas - h					199			0
testis - h					197			48
Salivary gland - h					195			0
HEP-2 cell TGF-β1 overexpression					193			0
HEP-2 cell TGF-β1 overexpression					179			0
Brain 1					81			0
Brain 2					50			0
lymph node - h					57			0
lung - h					54			0
kidney - h					53			309
heart - h					51			0
testis - h					49			0
testis - h					79			524
testis - h					81			71
HELA-293-031899					83			874
HELA-293-031899					80			181
HELA-293-031899					88			0
HELA-293-031899					90			81
HELA-293-031899					94			0
HELA-293-031899					95			120
HELA-293-031899					146			8
HELA-293-031899					148			86
HELA-293-031899					150			284
HELA-293-031899					152			0
HELA-293-031899					154			127
HELA-293-031899					156			0
HELA-293-031899					158			185
HELA-293-031899					160			0
HELA-293-031899					162			0
HELA-293-031899					164			0
HELA-293-031899					166			0
HELA-293-031899					168			0
HELA-293-031899					170			0
HELA-293-031899					172			0
HELA-293-031899					174			0
HELA-293-031899					176			0
HELA-293-031899					178			0
HELA-293-031899					180			0
HELA-293-031899					182			0
HELA-293-031899					184			0
HELA-293-031899					186			0
HELA-293-031899					188			0
HELA-293-031899					190			0
HELA-293-031899					192			0
HELA-293-031899					194			0
HELA-293-031899					196			0
HELA-293-031899					198			0
HELA-293-031899					200			0
HELA-293-031899					202			0
HELA-293-031899					204			0
HELA-293-031899					206			0
HELA-293-031899					208			0
HELA-293-031899					210			0
HELA-293-031899					212			0
HELA-293-031899					214			0
HELA-293-031899					216			0
HELA-293-031899					218			0
HELA-293-031899					220			0
HELA-293-031899					222			0
HELA-293-031899					224			0
HELA-293-031899					226			0
HELA-293-031899					228			0
HELA-293-031899					230			0
HELA-293-031899					232			0
HELA-293-031899					234			0
HELA-293-031899					236			0
HELA-293-031899					238			0
HELA-293-031899					240			0
HELA-293-031899					242			0
HELA-293-031899					244			0
HELA-293-031899					246			0
HELA-293-031899					248			0
HELA-293-031899					250			0
HELA-293-031899					252			0
HELA-293-031899					254			0
HELA-293-031899					256			0
HELA-293-031899					258			0
HELA-293-031899					260			0
HELA-293-031899					262			0
HELA-293-031899					264			0
HELA-293-031899					266			0
HELA-293-031899					268			0
HELA-293-031899					270			0
HELA-293-031899					272			0
HELA-293-031899					274			0
HELA-293-031899					276			0
HELA-293-031899					278			0
HELA-293-031899					280			0
HELA-293-031899					282			0
HELA-293-031899					284			0
HELA-293-031899					286			0
HELA-293-031899					288			0
HELA-293-031899					290			0
HELA-293-031899					292			0
HELA-293-031899					294			0
HELA-293-031899					296			0
HELA-293-031899					298			0
HELA-293-031899					300			0
HELA-293-031899					302			0
HELA-293-031899					304			0
HELA-293-031899					306			0
HELA-293-031899					308			0
HELA-293-031899					310			0
HELA-293-031899					312			0
HELA-293-031899					314			0
HELA-293-031899					316			0
HELA-293-031899					318			0
HELA-293-031899					320			0
HELA-293-031899					322			0
HELA-293-031899					324			0
HELA-293-031899					326			0
HELA-293-031899					328			0
HELA-293-031899					330			0
HELA-293-031899					332			0
HELA-293-031899					334			0
HELA-293-031899								

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Table 3 (cont'd)

Tissue	Tumor origin	Normal origin	Tumor - 1a	Tumor cells	Normal	Gene	EC	SEQ ID NO
Cal-3				178				1
FS-6				183				2
1-47D				171				3
Kan-3				181				4
CRS 1441 RNA 8/90				183				5
7811 untreated + Dexam				184				6
H8 poly A+				186				7
H8 poly A+				190				8
ACM				200				9
UACC-42				202				10
MDA-MB-435				204				11
MDA-MB-435				206				12
MDA-MB-435				208				13
MDA-MB-435				210				14
MDA-MB-435				212				15
MDA-MB-435				214				16
MDA-MB-435				216				17
MDA-MB-435				218				18
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MDA-MB-435				602				210
MDA-MB-435				604				211
MDA-MB-435				606				212
MDA-MB-435								

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Table 3 (cont'd)

Tissue	Tumor type	Pathology	Tumor size	Tumor cells	Normal	Exon	p53	SEQ ID NO
MCF-7	153							0
MCF-7ADR-RES	151							0
MCF-7	149							0
MCF-7	147							0
MCF-7	145							0
MCF-7	144							0
MCF-7	143							0
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MCF-7	5							0
MCF-7	4							0
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MCF-7	2							0
MCF-7	1							0
MCF-7	0							0



Table 4

Gene Name	SP ID#	na ID#	aa	Family	Group	Length_AA	Extra-Catalytic Domains (Amino acid positions)
X69117_h_beta_adrene	H	1	122	AGC	GRK	688	Regulator of G protein signalling domain 54-175; PH domain 559-652
AA144574_m	M	2	123	AGC	GRK	378	PH domain 249-337
AA210925_h	H	9	130	AGC	PKC	978	Phorbol esters/diacylglycerol binding domain (C1 domain) 238-287; PH domain 497-577
AA316804_h	H	11	132	AGC	PKC	890	Phorbol esters/diacylglycerol binding domain (C1 domain) 155-204 and 272-321; PH domain 417-532
AA887783_h	H	21	142	AGC	SGK	446	PX domain 13-120
AA021445_h3	H	32	152	CAMK	EMK	1311	Vitamin K-dependent carboxylation/gamma-carboxyglutamic (GLA) domain 1072-1113
R31237_1_h_AAC3348	H	34	154	CAMK	EMK	729	UBA domain 327-365
408786.5_h	H	36	156	CAMK	EMK	1330	PAS domain 133-186, 247-280, 354-386
Z38720_h	H	41	161	CAMK	MLCK	874	WD domain, G-beta repeat 674-711
SGK088_h	H	42	162	CAMK	Trio	2287	Immunoglobulin domain 1-62, 97-153, 221-277, 518-578, 1617-1678; Fibronectin type III domain 301-390, 1697-1779
R19772_h	H	44	164	CAMK	Trio	1287	RhoGEF domain 235-405; Fibronectin type III domain 870-955; Immunoglobulin domain 786-851; PH domain 419-528
17000139601197_h_IRA	H	76	195	Other	IRAK	596	Death domain 26-108
AA088547_h	H	78	197	Other	IRE	922	PQQ enzyme repeat 39-76
AA232253_h	H	82	201	Other	MLK	800	SAM domain (Sterile alpha motif) 337-408
AA599286_h	H	89	208	Other	SLOB	649	PX domain 16-122
AA838348_h	H	113	232	STE	NEK	836	Regulator of chromosome condensation (RCC1) 387-427, 427-480, 483-532, 598-650
PAK6_h	H	115	234	STE	STE20-02	719	P21-Rho-binding domain 11-69

## FIGURE 1A

SEQ ID NO: 122\_X69117\_H BARK2\_H  
MADLEAVLADVSYLMAMEKSKATPAARASKRIVLPEPSIRSVMQKYLAERNEITFDKIFN  
QKIGFLLFKDFCLNEINEAVPQVKFYEEIKEYEKLDNEEDRLCRSRQIYDAYIMKELLSC  
SHPFSKQAVEHVQSHLSKKQVTSTLFPQYIEEICESLRGDI FQKFMESDKFTRFCQWKNV  
ELNIHLTMNEFSVHRIIGRGGFGEVYGCRKADTGKMYAMKCLDKKRIKMKQGETLALNER  
IMLSLVSTGDCPFIVCMTYAFHTPDKLCFILDLMNGGDLHYHLSQHGVFSEKEMRFYATE  
IILGLEHVHNRFFVYRDLKPANILLDEHG HARISDLGLACDFS KKKPHASVGTHGYMAPE  
VLQKGTAYDSSADWFSLGCMFLKLLRGHSPFRQHKTCDKHEIDRMTLTVNVELPDTFSPE  
LKSLLLEGLLQRDVSKRLGCHGGGSQEVKEHSFFKGVDWQH VYLQKYPPLIPPRGEVNAA  
DAFDIGSFDEEDTKGIKLLDCDQELYKNFPLVISERWQQEVTETVYEAVNADTDKIEARK  
RAKNKQLGHEEDYALGKDCIMHGYMLKLGNPFLTQWQRRYFYLF PNRLEWRGEGESRQNL  
LTMEQILSVEETQIKDKKCILFRIKGGKQFVLQCESDPEFVQWKKE LNETFKEAQRLLRR  
APKFLNKPRSGTVELPKPSLCHRNSNGL

SEQ ID NO: 123\_AA144574\_M BARK2\_M  
CFVVYRDLKPANILLDEYGHVRIISDLGLACDFS KKKPHASVGTHGYMAPEVLQKGT CYDS  
SADWFSLGCMFLKLLRGHSPFRQHKTCDKHEIDRMTLTVNVLQPD AFSPELRSLLEGLLQ  
RDVSQRLGCGGGGARELKEHIFFKGIDWQH VYLRYKYPPLIPPRGEVNAA DAFDIGSFDE  
EDTKGIKLLDCDQDLYKNFPLVISERWQQEVVETIYDAVNADTDKIEARKKAKNKQLGQE  
EDYAMGKDCIMHGYMLKLGNPFLTQWQRRYFYLF PNRLEWRGEGESRQSLLTMEQIMSVE  
ETQIKDRKCILLRIKGGKQFVLQCESDPEFAQWLKELTCTFNEAQRLLRRAPKFLNK PRA  
AILEFSKPPLCHRNSSGL

SEQ ID NO: 124\_AA826850\_H  
MGSSMSAATARRPVFDDKEDVNFDFH FQILRAIGKGSFGKVCIVQKRDTEKMYAMKYM NKQ  
QCIERDEVNRNVFRELEILQEIEHVFLVNLWYSFQDEEDMFMVVDLLLGGDLRYHLQQNVQ  
FSEDTVRLYICEMALALDYLRGQHI IHRDVKPDNILLDERGHAHLTDFNIATIIKDGERA  
TALAGTKPYMAPEIFXSFVNGGTGYSFEVDWWSVGMAYELLRGWRPYDIHSSNAVESLV  
QLFSTVSQYVPTWSKEMVALLRKLLTVNPEHRLSSLQDVQAAPALAGVLWDHLSEKRVE  
PGFVPNKGRHLHCDPTFELEEMILES RPLHKKKKRLAKNKS RDNSRDSSQSENDYLQDCLD  
AIQQDFVIFNREKLKRSQDLPREPLPAPESRDAAEPVEDEAERSALPMCGPICPSAGSG

SEQ ID NO: 125\_AA960957\_H  
MGGNHSHKPPVFDENEEVNFDFH FQILRAIGKGSFGKVCIVQKRDTKMYAMKYM NKQKCI  
ERDEVNRNVFRELQIMQGLEHPFLVNLWYSFQDEEDMFMVVDLLLGGDLRYHLQQNVH FTE  
GTVKLYICELALALEYLQRYHI IHRDIKPDNILLDEHG HVHITDFNIATVVKG AERASSM  
AGTKPYMAPEVFQVYMDRGPGYSYPVDWWSLGITAYELLRGWRPYEIH SVTPIDEILNMF  
KVERVHYSSTWCKGMVALLRKLLTKDPESRVSSLHDIQSVPYLADMNWD AVFKKALMPGF  
VPNKGRNLNCDPTFELEEMILES KPLHKKKKRLAKNRSRDGT KDSCPLNGHLQH CLETVRE  
EFIIFNREKLRRQQGQGSQLLD TDSRGGGQAQSKLQDGCNNNLLTHTCTRGCSS

SEQ ID NO: 126\_TBK1\_H  
MQSTSNHLWLLSDILGQATANVFRGRHKKTGDLFAIKVFNNISFLRPVDVQMREFEVLK  
KLNHNKIVKLF AIEEETTRHKVLIMEFCPCGSLYTVLEEPSNAYGLPESEFLIVLRD VV  
GGMNHLRENGIVHRDIKPGNIMRVIGEDGQSVYKLTDFGAARELEDDEQFVSLYGT EEYL  
HPDMYERAVLRKD HQKKYGATVDLWSIGVTFYHAATGSLPFRPFEGPRRNKEVMYKIITG  
KPSGAISGVQKAENGPIDWSGDMPVSCSLSRGLQVLLTPVLANILEADQEK CWGFDQFFA  
ETSDILHRMVIHVFSLQQMTAHKIYIHSYNTATIFHEL VYKQTKIISNQELIYEGRR LV  
LEPGRLAQHF PKTTEENPIFVVSREPLNTIGLIYEKISLPKVHPRYDL DGDASMAKAITG  
VVCYACRIASTLLLYQELMRKGIRWLI ELIKDDYNETVHKKTEVVITLDFCIRNIEKTVK

## FIGURE 1B

VYEKLMKINLEAAELGEISDIHTKLLRLSSSQGTIETSLQDIDSRLSPGGSLADAWAHQE  
 GTHPKDRNVEKLQVLLNCMTEIYYQFKDKAERRLAYNEEQIHKFDKQKLYYHATKAMTH  
 FTDECVKKYEAFLNKSEEWIRKMLHLRKQLLSLTNQCFDIEEEVSKYQEYTNELQETLPQ  
 KMFTASSGIKHTMTPIYPSSNTLVEMTLGMKKLKEEMEGVVKELAENNHILERFGSLTMD  
 GGLRNVDCI

SEQ ID NO: 127\_AA305176\_H  
 MDPTAGSKKEPGGGAATEEGVNRIAVPKPPSIEEFSIVKPISRGAFGKVYLQKGKGLYA  
 VKVVKKADMINKNMTHQVQAERDALALSKSPFIVHLYYSLQSANNVYLVMEYLIGGDVKS  
 LLHIYGYFDEEMAVKYISEVALALDYLHRHGIHRDLKPDNMLISNEGHIKLTDFGLSKV  
 TLNRDINMMDILTPSPMAKPRQDYSRTPGQVLSLISSLGFTPIAEKNQDPANILSACLS  
 ETSQLSQGLVCPMSVDQKDTTPYSSKLLKSCLETVASNPGMPVKCLTSNLLQSRKRLATS  
 SASSQSHTFISSVESECHSSPKWEKDCQV

SEQ ID NO: 128\_AA116841\_M  
 TRPIPWPEGEEKLSDNAQSAMDMLLTIDDSKRAGMRELKQHPLFSEVDWENLQHQTMPFV  
 PQPDDDETDSYFEARNNAQHLTVSGFSL

SEQ ID NO: 129\_AA256100\_H  
 MAMTAGTTTTFPMNSNHTRERVTVAKLTLENFYSNLILQHEERETRQKKLEVAMEEEGLAD  
 EEKKLRRSQHARKETEFRLRLKRTLGLDDFESLKVIGRGAFGEVRLVQKKTGHIYAMKI  
 LRKSDMLEKEQVAHIRAERDILVEADGAWVVKMFYSFQDKRNLYLIMEFLPGGDMMTLLM  
 KKDTLTEEETQFYISETVLAIDAIHQLGFIHRDIKPDNLLLDAGHVKLSDFGLCTGLKK  
 AHRTEFYRNLTNPPSDFSQNMNSKRKAETWKKNRRQLAYSTVGTDPYIAPEVFMQTGY  
 NKLCDWWSLGVIMYEMLIYPPFCSETPQETRYKVMNWKETLVFPPEVPISEKAKDLILR  
 FCIDSENRIKNSGVVEIKGHPFFEGVDWEHIRERPAAPIEIKSIDDSNFDDFPESDIL  
 QVPNTTEPDYKSKDWVFLNYTYKRFEGLTQRGSIPTYMKAGKL

SEQ ID NO: 130\_AA210825\_H  
 DSLLPTPALGTPLPIWPVGSRLTPLSLESTRSPTQRLLPSTPKDPAILRSPPPARSFLG  
 SPLSHLLTRSRGSRTOGPPGPPGGSRVGSRRAVPGLPPWPPPPHYAGLPGSPGPGSP  
 PPGGLELQSPPLLPQIPAPGSGVSFHIQIGLTREFVLLPAASELAHVQLACSIQVQKF  
 PECGFYGLYDKILLFKHDPTSANLLQLVRSSGDIQEGDLVEVVLSASATFEDFQIRPHAL  
 TVHSYRAPAFCDHCGEMLFGLVRQGLKCDGGLNYHKRCAFSIPNNCSGARKRRLSSTSL  
 ASGHSVRLGTSESLPCTAEELSRSTTELLPRRPPSSSSSSSASSYTGRPIELDKMLLSKV  
 KVPHTFLIHSYTRPTVCQACKLLKGLFRQGLQCKDKFNCHKRCATRVNDCLGEALIN  
 GDVPMEEATDFSEADKSALMDESEDGVI PGSHSENALHASEEEEGEGGAQSSSLGYIPL  
 MRVVQSVRHTTRKSSTTLREGWVHYSNKDTLRKRHYWRLDCKCITLQNTTNRYYKEI  
 PLSEILTVEAQNFSLVPPGTNPHCFEIVTANATYFVGEMPGGTGPGPSGQGAEAARGLX  
 ETAIRQALMPVILQDAPSAPGHAPHRQASLSISVSNSQIQENVDIATVYQIFPDEVLGSG  
 QFGVVYGGKHKRTGRDVAVKVIDKLRFPPTKQESQLRNEVAILQSLRHPGIVNLECMFETP  
 EKVFVMEKHLHGDMLEMILSSEKGRLEPRLTKFLITQILVALRHLHFKNIVHCDLKPENV  
 LLASADFPQVKLCDFGFARIIGEKSFRRSVVGTPAYLAPEVLLNQGYNRSLDMWSVGVI  
 MYVSLSGTFPFNEDEDINDQIQNAAFMYPASPWSHISAGAILINNLLQVKMRKRYSVDK  
 SLSHPWLOEYQTWLDLRELEGKMGERYITHESDDARWEQFAAEHPLPGSGGLPTDRDLGGA  
 CPPQDHDMQGLAERISVL

SEQ ID NO: 131\_AA127299\_H  
 IQFIIVGAKDLLAMDSNGLSDPYIKITNLSQTKVIKKTLTPTWNETFFVHFPEKTTLEL  
 ECWDHDTFSDDFIGKASISLAEIPALAEVDMWIDMKTCKGEFAGK



## FIGURE 1C

SEQ ID NO: 132\_AA316804\_H  
 MSANNSPPSAQKSVLPTAIPAVLPAASPCSSPKTGLSARLSNGSFSAPSLTNSRGSVHTV  
 SFLQLQIGLTRESVTIEAQELSLSAVKDLVCSIVYQKFPECGFFGMYDKILLFRHDMNSEN  
 ILQLITSADEIHEGDLVEVLSALATVEDFQIRPHTLYVHSYKAPTFCDYCGEMLWGLVR  
 QGLKCEGCGLNYHKRCAFKIPNNCSGVRKRRLSNVSLPGPGLSVPRPLQPEYVALPSEES  
 HVHQEPSKRIPSWSGRPIWMEKMVMCRVKVPHTFAVHSYTRPTICQYCKRLLKGLFRQGM  
 QCKDCKFNCHKRCASKVPRDCLGEVTFNGEPSSLGTDTDIPMDIDNNDINSDSSRGLDDT  
 EEPSPPEDKMFFLDPSDLDERDEEAVKTI SPSTSNNIPLMRVVQSIKHTKRKSSTMVKE  
 GWMVHYTSRDNLKRHYWRDLDSKCLTLFQNESGSKYYKEIPLSEILRISSPRDFTNISQ  
 SNPHCFEII TDTMVYFVGENNGDSSSNPVLAATGVGLDVAQSWEKAIRQALMPVTPQASV  
 CTSPGQGDHKLSTSI SVSNCCI QENVDISTVYQIFADEVLGSGQFGIVYGGKHKRKTGR  
 DVAIKVIDKMRFP TKQESQLRNEVAILQNLHHPGIVNLECMFETPERVFVMEKLGHDML  
 EMILSSEKSR LPERITKFMVTQILVALRNLHFKNIVHCDLKPENVLLASAEPFPQVKLCD  
 FGFARIIGEKSFRRSVVGTPAYLAPEVLRSGYNRSLDMWSVGVI IYVSLSGTFPFNEDE  
 DINDQIQNAAFMYPPNPWREISGEAIDLINLLQVKMRKRYSDKSLSHPWLDYQTLWD  
 LREFETRIGERYITHESDDARWEIHAYTHNLVYPKHFIMAPNPDDMEEDP

SEQ ID NO: 133\_PKNBETA\_H  
 MEEGAPRQPGPSQWPPPEDEKEVIRRAIQKELKIKEGVENLRRVATDRRHLGHVQQLLRSS  
 NRRLEQLHGELRELHARILLPGPGPGAEPVASGPRPWAEQLRARHLEALRRQLHVELKV  
 KQGAENMTHTCASGTPKERKLLAAQQLRDSQLKVALLRMKISSLEASGSPEPGPELLA  
 EELQHRHLHVEAAVAEGAKNVVLLSSRRTQDRKALAEQAQLQESSQKLDLLRLALEQLL  
 EQLPPAHLRSRVRELRAAVPGYPQPSGTPVKPTALTGTLOVRLGCEQLLTAVPGRSP  
 AAALASSPSEGWLRTKAKHQGRGELASEVLAVLKVDNRVVGQTGWGQVAEQSWDQTFVI  
 PLERARELEIGVHWRDWRQLCGVAFLRLEDFLDNACHQLSLSLVPQGLLFAQVTFCDPVI  
 ERRPRLQRQERIFSKRRGQDFLRRSQMNLGMAAWGRLVMNLLPPCSPSTISPPKGCPR  
 PTTLREASDPATPSNFLPKKTPLGEEMTPPPKPRLYLPOEPTSEETPRTRKPHMEPRTR  
 RGPSPASPTRKPPRLQDFRCLAVLGRGHFGKVLLVQFKGTGKYAIAKALKKQEVLSRDE  
 IESLYCEKRILEAVGCTGHPFLSLLVCFQTSSHARFVTEFVPGDLMQIHEDVFPEPQ  
 ARFYVACVVLGLQLHEKKIIYRDLKLDNLLLDAAQGLFKIADFGLCKEGIGFGDRTSTFC  
 GTPEFLAPEVLTQEAYTQAVDWWALGVLLYEMLVGECPPFGDTEEEVFDCIVNMDAPYPG  
 FLSVQGLEFIQKLLQKCPEKRLGAGEQDAEEIKVQPPFRTTNWQALLARTIQPPFVPTLC  
 GPADLRYFEGEFTGLPPALTPPAPHSLLTARQQAARDFDFVSERFLEP

SEQ ID NO: 134\_AI021023\_M PKNBETA\_M  
 LKWDNLLLDAAQGLFKIADFGLCKEGIGFGDRTSTFCGTPEFLAPEVLTQEAYTRAVDWWG  
 LGVLLYEMLVGECPPFGDTEEEVFDCIVNMDAPYPGFLSVQGLEFIQKLLQKCPEKRLGA  
 GEQDAEEIKVQPPFRTTNWQALLARTIQPPFVPTLCGPADLRYFEGEFTGLPPALTPPAP  
 HSLLTARQQAARDFDFVSERFLEP

SEQ ID NO: 135\_H19102\_H  
 GGNIRGPWARGWKS LWTGLGTIRSDLEELWELRGHHYHLHQLKPAVVLVEKPLPEWPVP  
 QFINFLPEFPPIRPIRGQQQLKILGLVAKGSFGTVLKVLDTQKAVFAVKVVPKVKVLQR  
 DTVRQCKEEVSIQRQINHPFVHSLGDSWQGRHLFIMCSYCSTDLYSLWSAVGCFPEASI  
 RLFAAELVLVLCYLHDLGIMHRDVKMENILLDERGHLKLTDFGLSRHVPQGAQAYTICGT  
 LQYMAPEVLSGGPYNHAADWWSLGVLLFSLATGKFPVAAERDHSVAMLASVTHSDSEIPAS  
 LNQGLSLLLHELLCQNLHRLRYLHHPFQVHPFFRGVAFDPELLQKQPVNFVTETQATQPS  
 SAETMPFDDFDCDLESFLLYPIPA

## FIGURE 1D

SEQ ID NO: 136\_AA476563\_H

MEFFRIDSKDSASELLGLDFGEKLYSLKSEPLKPFFTLPDGDSASRSFNTSESKVEFKAQ  
DTISRGSDDSVPVISFKDAAFDDVSGTDEGRPDLLVNLPGELESTREAAAMGPTKFTQTN  
IGI IENKLLLEAPDVLCLRLSTEQCQAHEEKGIEELSDPSGPKSYSITEKHYAQEDPRMLF  
VAAVDHSSSGDMSLLPSSDPKFQGLGVVESAVTANNTESLFRI CSPLSGANEY IASTDT  
LKTEEVLLFTDQTDLLAKEEPTSLFQRDSETKGESGLVLEGDKEIHQIFEDLDKKLALAS  
RFYIPEGCIQRWAAEMVVALDALHREGIVCRDLNPNNILLNDRGHIQLTYFSRWSEVEDS  
CDSDAIERMYCAPEVGAI TEETEACDWWSLGAVLFELLTGKTLVECHPAGINTHTTLNMP  
ECVSEEARSLIQQLLQFNPLERLGAGVAGVEDIKSHPFFTPVDWAELMR

SEQ ID NO: 137\_AA626690\_H

MLPFAPQDEPWDREMEVFSGGGASSGEVNGLMVDEPMEEGEADSCHDEGVVKEIPITHH  
VKEGYEKADPAQFELLKVLGQGSFGKVFLVRKKTGPDAGQLYAMKVLKKASLKVRDRVRT  
KMERDILVEVNHPFIVKLHYAFQTEGKLYLILDFLRGGDVFTRLSKEVLFTTEEDVKFYLA  
ELALALDHLHLQIGIVYRDLKPENILLDEIGHIKLTD FGLSKESVDQEKKAYSFCGTVEYM  
APEVVNRRGHSQSADWWSYGVL MFEMLTGTL PFQKDRNETMNMILKAKLGMPQFLSAEA  
QSLLRMLFKRNPANRLGSEGVEEIKRHLFFANIDWDKLYKREVQPPFKPASGKPD DTF CF  
DPEFTAKTPKDS PGLPASANAHQLFKGFSFVATSIAEEYKITPITSANVLP I VQINGNAA  
QFGEVYELKEDIGVGSYSVCKRCIHATTNMEFAVKI IDKSKRDPSEEIEILMRYGQHPNI  
ITLKDVFDDGRYVYLVTDLMKGGELLDRI LKQKCF SEREASDILYVISKTVDYLHCQGVV  
HRDLKPSN ILYMDESASADSIRICDFGFAKQLRGENGLLLTPCYTANFVAPEVLMQQGYD  
AACDIWSLGVLFYTMLAGYTPFANGPNDTPEEILLRIGNGKFSLSGGNWDNISDGAKDLL  
SHMLHMDPHQRYTAEQILKHSWITHRDQLPNDQPKRNDVSHVVKGAMVATYSALHTKTFO  
PVLEPVAASSLAQRRSMKKRTSTGL

SEQ ID NO: 138\_AA215680\_H

MSLVACECLPSPGLEPEPCSRARSQAHVYLEQIRNRVALGV PDMTKRDYLVDAATQIRLA  
LERDVSEDEYEA AFNHYQNGVDVLLRG I HVDPNKERREAVKLKITKYLRRAE E I FNCHLQR  
PLSSGASPSAGFSSRLRLRPIRTLSSAVEQLRGCRVVGVI EKVLVQDPATGCTFVVKSLP  
RCHMVSRERLTII PHGVPYMTKLLRYFVSEDSIFLHLEHVQGGTLWSHLLSQAHSRHSGL  
SSGSTQERMKAQLNPHLNLTPARLP SGHAPGQDRIALEPRTSPNLLLAGEAPSTRPQR  
EAEGEPTARTSTSGSSDLPKAPGGHLHLQARRAGQNSDAGPPRGLTWVPEGAGPVLGGCG  
RGMDQSCLSADGAGRGCGRATWSVREEQVKQWAAEMLVALEALHEQGVLCRDLHPGNLLL  
DQAGHIRLTYFGQWSEVEPQCCGEAVDNLYSAPEVGGISELTEACDWWSF GSLLYELLTG  
MALSQSHPSGIIQAHTQLQLPEWLSRPAASLLTELLQFEPTRR LGMGEGGVSKLKSHPFFS  
TIQWSKLVG

SEQ ID NO: 139\_SGK\_H

MTVKTEAAKGTLYSRMRGMVAILIAFMKQRRMGLNDFIQKIANN SYACKHPEVQSILKI  
SQPQEP ELMNANPSPPPSPSQQINLG PSSNPHAKPSDFHFLKVIGKGSFGKVLLARHKA E  
EVFYAVKVLQKKAILKKKEEKHIMSERNVLLKNVKHPFLVGLHFSFQTADKLYFVLDYIN  
GGELFYHLQRERCFLEPRARFYAAEIASALGYLHSLNIVYRDLKPENILLDSQGHIVLTD  
FGLCKENIEHNSTTSTFCGTPEYLAPEVLHKQPYDRTVDWWCLGAVLYEMLYGLPPFYSR  
NTAEMYDNILNKPLQLKPNI TNSARHLLLEGLLQKDRTKRLGAKDDFMEIKSHVFFSLINW  
DDLINKKITPPFNPNVSGPNELRHFDPEFTEEPVPNSIGKSPDSVLVTASVKEAAEAFLG  
FSYAPPTDSFL

SEQ ID NO: 140\_AA107515\_M

MTVKAEAAARSTLYSRMRGMVAILIAFMKQRRMGLNDFIQKIASNTYACKHAEVQSILKM  
SHPQEP ELMNANPSPPPSPSQQINLG PSSNPHAKPSDFHFLKVIGKGSFGKVLLARHKA E

## FIGURE 1E

EVFYAVKVLQKKAILKKKEEKHIMSERNVLLKNVKHPFLVGLHFSFQTADKLYFVLDYIN  
GGELFYHLQRERCFLEPRARFYAAEIASALGYLHSLNIVYRDLKPENILLDSQGHIVLTD  
XFQLRRIEHNGTTSTFCGTPEYLAPVLRKEPYDRAVDWWCLGAVLYEMLYGLPPFYSRN  
TAEMYDNILNKPLQLKPNITNSARHLLLEGLLQKDRTKRLGAKDDFMEIKSHIFFSLINWD  
DLINKKITPPFNPVSGPSDLRHFDPFTEEPVPSSIGRSPDSILVTASVKEAAEAFGLG  
SYAPPVDSFL

SEQ ID NO: 141\_AA109508\_M  
HLQRERRFLEPRARFYAAEIVASAIGYLHSLNIIYRDLKPENILLDCQGHVVLTDGFLCKE  
GVEPEDTTSTFCGTPEYLAPVLRKEPYDRAVDWWCLGAVLYEMLHGLPPFYSDVSQMY  
ENILHQPLQIPGGRTVAACDLLQSLHKKDQORQLGSKADFLEIKNHVFFSPINWDDLYHK  
RLTPPFNPVNTGPADLKHFDPEFTQEAVSKSIGCTPDTVASSSGASSAFLGFSYAPEDDD  
ILDC

SEQ ID NO: 142\_AA887783\_H  
MQRDHTMDYKESCPVXIPSSDEHREKKKRFVYKVLVSVGRSEWVFRRYAEFDKLYNT  
LKKQFPAXALKIPAKRIFGDNFDPDFIKQRRAGLNEFIQNLVRYPELYNHPDVRAFLQMD  
SPKHQSDPSEDEDERSSQKLHSTSQNINLGPSPGNPHAKPTDFDFLKVIGKGSFGKVLAK  
RKLDGKFYAVKVLQKKIVLNRKEQKHMAERNVLLKNVKHPFLVGLHYSFOTTEKLYFVL  
DFVNGGEGHVVLTDGFLCKEGIAISDTTTFCTGTPEYLAPVIRKQPYDNTVDWWCLGAV  
LYEMLYGLPPFYCRDVAEMYDNILHKPLSLRPGVSLTAWSI LELLEKDRQNLGAKEDF  
LEIQNHPPFESLSWADLVQKKIPPPFNPVAGPDDIRNFDTAFTETVPYSVCVSSDYSI  
VNASVLEADDAFVGFSYAPPSIDLFL

SEQ ID NO: 143\_R47805\_H  
MAHQGTGIHATEELKEFFAKARAGSVRLIKVVI EDEQLVLGASQEPVGRWDQDYDRAVLPL  
LDAQQPCYLLYRLDSQNAQGFEWLFLAWSPDNVRLKMLYAATRATVKKEFGGGHIKDE  
LFGTVKDDLSFAGYQKHLSSCAAPAPLTS AERELQIRINEVKTEISVESKHQTLQGLAF  
PLQPEAQRALQQLKQKMVNYIQMKLDERETIELVHTEPTDVAQLPSRVPRDAARYHFFL  
YKHTHEGDPLESVVFYISMPGYKCSI KERMLYSSCKSRLLDSVEQDFHLEIAKKIEIGDG  
AELTAEFLYDEVHPKQAHAFKQAFAPKPGPGGKRGHKRLIRGPGENGDD

SEQ ID NO: 144\_H60215\_H  
MSKLRMKRRASDRGAGETSARAKALGSGISGNNAKRAGPFILGPRLGNSPVPSIVQCLAR  
KDGTDDFYQLKILTLEERGDQGI ESQEERQGMILLHTEYSLLSLLHTQDGVVHHHGLFQD  
RTCEIVEDTESSRMVKKMKKRICLVLDCLCAHDFS DKTADLINLQHYVIKEKRLSERETV  
VIFYDVVRVVEALHQKNI VHRDLKLGNMVLNKRTHRITITNFCLGKHLVSEGDLLKDQRG  
SPAYISPDLVSGRPYRGKPSDMWALGVVLF TMLYGQFPFYDSIPQELFRKIKAAEYTIPE  
DGRVSENTVCLIRKLLVLDPQORLAAADVLEALS AIIASWQSLSSLSGPLQVVPDIDDQM  
SNADSSQEAKVTEEC SQYEFENYMRQQLLLAEKSSIHDTRS WVPKRQFGSAPPVRRLGH  
DAQPMTSLDTAILAQRYLRK

SEQ ID NO: 145\_SGK324\_H  
MASTRSIELEHFEERDKRPRPGSRRGAPSSSGGSSSSGPKGNGLIPSPAHS AHCSFYRTR  
TLQALSSEKKAKKARFYRNGDRYFKGLVFAISSDRFRSFDALLIELTRSLSDNVNLPQGV  
RTIYITIDGSRKVTSLDELLEGESYVCASNEPFRKVDYTKNINPNWSVNI KGGTSRALAA  
SSVKSEVKESKDFIKPKLVTVIRSGVKPRKAVRILLNKKTAHSFEQVLT DITEAIKXASG  
VVKRLCTLDGKQVRVTCVHLPDFFGDDVFIACGPEKFRYAQDDFVL DHSECRVLKSSYS  
RSSAVKYSGSKSPGPSRRSQISAHGRSSSNVNGGPELDRCISPEGVNGNRCSESSTLLEK  
YKIGKVIGDGNFAVVKECIDRSTGKEFALKIIDKAKCCGKEHLIENEVSILRRVKHPNII

## FIGURE 1F

MLVEEMETATELFLVMELVKGGDLFDAITSSTKYTERDGSAMVYNLANALRYLHGLSIVH  
 RDIKPENLLVCEYPDGTSLKLGDFGLATVVEGPLYTVCGTPTYVAPXIIAETGYGLKVD  
 IWAAGVITYILLCGFPFRSENNLQEDLFDQILAGKLEFPAPYWDNITDSAKELISQMLQ  
 VNVEARCTAGQILSHPWVSDASQENNMQAEVTGKLKQHFNNALPKQNSTTTGVSVMVS  
 GRRQVWPDCGAGLEVFEFGSRELPSHGSWCLP

SEQ ID NO: 146\_W30246\_M SGK324\_M  
 TKSSSSSPTSPGSFRGLKISAQGRSSSNVNGGPELDRCLSPGVNGNRCSESFPILLEKYR  
 IGKVIKGNFAVVKECVDRTYTGKEFALKIIDKAKCCGKEHLIENEVSILRRVKHPNII ML  
 VEEMETATDLFLVMELVKGGDLFDAITSSTKYTERDGSAMVYNLANALRYLHLSIVHRD  
 IKPENLLVCEYPDGTSLKLGDFGLATVVEGPLYTVCGTPTYVAPEIIAETGYGLKVDVW  
 AAGVITYILLCGFPFRSENNLQEDLFDQILAGKLEFPAPYWDNITDPCVCFRKCL

SEQ ID NO: 147\_AA383293\_H  
 PAAKRVVYRNGDPFFPGSQLVVTQRRFPTMEAFLEVTSAVQAPLAVRALYTPCHGHPV  
 TNLADLKNRGQYVAAGFERFHKLPYQAFCLSVFRNGDLVSPFFSLKLSQAASQDWETVL  
 KLLTEKVKLQSGAVRLCTLEGLPLSAGKELVTGHYYVAVGEDEFKDLPPALSTRGLLAA  
 GNEAHLRSVGTVAGSPKPLGRKAKKETCLIVTLTKYQQSETSRDGQSFPSPGVIGVYGA  
 PHRRKETAGALEVADDEDTQTEEPLDQRAAQIVEQVTCLQDFFGDDDFIACGPEKFRYA  
 QDDFVLDSRRRLREHQAGFEKLRRTRGEEKEAEKEKKPCMSGGRRMTLRDDQPAKLEK  
 EPKTRPEENKPERPSGRKPRPMGI IAANVEKHYETGRVIGDGNFAVVKECRHRETRQAYA  
 MKIIDKSRLKGGKEDMVDSEILIIQSLSHPNIVKLHEVYETDMEIYLIILEYVQGGDLFDAI  
 IESVKFPEPDAAALMIMDLCKALVHMHDKSI VHRDLKPENLLVQRNEDKSTTLKLADFGLA  
 KHVVVRPIFTVCGTPTYVAPEILSEKGYGLEVDMWAAGVILYILLCGFPFRSPXXGDQDE  
 LFNIIQLGHFEFLPPYWDNISDAAKDLVSRLLVDPKKRYTAHQVLQHPWIETAGKTNTV  
 KRQKQVSPSSDGHFRSQHKRVVEQVS

SEQ ID NO: 148\_AA197883\_M  
 MPTAPVLRPPPPPATPAPPAPSRPAPPIPGHRGPCDHSCLKCLSSKISERKLPGPWLPAGR  
 GPLEKPVLGPRGAVMPLFSPQSSLHSVRAEHSPLKPRVTVVKLGGQPLRKATLLLNRRS  
 VQTFEQLLSDISEALGFPRWKNDVRKLF TLKGREVKSVDFFREGDAFIAMGKEPLTLK  
 SIQLAMEELYPKNRALALAPHSRVSPRLRSRLPSKLLKGSHRCGEAGSYSAEMESKAVS  
 RHQGTSTVLAPEDKARAQKWVRGKQSESEPGGPPSPGAATQEETHASGEKHLGVEIEKTS  
 GEIVRCEKCKRERELQLGLQREPCPLGTSELDLGRAQKRDSEKLVRTKSCRRPSKAKFTD  
 GEEGWKGDSHRGSPRDPPEMRRPNSNSDKKEIRGSESQDSYPQAPKAQKDFVEGPPAV  
 EEGPIDMRREDRHTCRSKHAAWLRRQQAEPPQLPRTRGEEKQAEHEKKPGGLGERRAPE  
 KESKRKLEEKRPERPSGRKPRPKGII SADVEKHYDIGGVIGDGNFATVKECRHRETRQAY  
 AMKMIDKSQKGGKEDI VDSEILIIQSLSHPNIVKLHEVYETEAEIYLIMEYVQGGDLFDA  
 IVENVKFPEPEAAVMITDLCKAFVHMHDKNIVHRDVKPENLLVQRNEDKSI TLKLADFG  
 AKYVVRPIFTVCGTPTYVAPEILSEKGYGLEVDMWAAGVILYILLCGFPFRSPERDQDE  
 LFNIIQVGQFEFLSPYWDNISDAAKDLVRNLLEVDPKKRYTAEQVLQHPWIEMVGHNTG  
 NSQKEESPNSLGHFQSQHKKVAEQMP

SEQ ID NO: 149\_DRAK2\_H  
 MSRRRFDCRSISGLLTTPQIPIKMFNNFYILTSKELGRGKFAVVRQCISKSTGQEYA  
 AKFLKKRRRGQDCRAEILHEIAVLELAKSCPRVINLHEVYENTSEIILILEYAAGGEIFS  
 LCLPELAEMVSENDVIRLIKQILEGVYYLHONNIVHLDLKPQNILLSSIYPLGDIKIVDF  
 GMSRKIGHACELREIMGTPEYLAPEILNYDPITTATDMWNIGIIAYMLLTHTSPFVGEDN  
 QETYLNI SQVNDYSEETFSSVSQLATDFIQSLLVKNPEKRPTAEICLSHSLWQQWDFEN

## FIGURE 1G

LFHPEETSSSSQTQDHSVRSSSEDKTSKSSCNGTCGDREDKENI PEDSSMVSKRFRFDDSL  
PNPHELVSDLLC

SEQ ID NO: 150\_W44160\_M\_DRAK2\_M  
MSRRRFDCRSVSGLLTTTPQTPIKTENFNNFYTLTPKELGRGKFAVVRQCISKSTGQEYA  
AKSLKKRRRGQDCRAEILHEIAVLELARSCPHVINLHEVYENATEIILVLEYAAGGEIFN  
LCLPELAEMVSENDVIRLIKQILEGVHYLHQNIVHLDLKPQNILLSSIIYPLGDIKIVDF  
GMSRKIGNASELREIMGTPEYLAPEILNYDPIITTATDMWNIGIIAYMLLTHTSPFVGEDN  
QETYNISQVNVYSEEMFSSVSQLATDFIQSLLVKNPEKRPTAESCLSHSWLQQWDFGS  
LFHPEETSGSSQIQDLTLRSSEKTSKSSCNGSCGAREDKENI PEDGSLVSKRFRFDDSL  
PSPHELVPDLFC

SEQ ID NO: 151\_H01248\_H, DRAK1\_H  
MIPLEKPGSGGSSPGATSGSGRAGRLSGPCRPPPPQARGLLTEIRAVVRTEPFQDGYS  
LCPGRELGRGKFAVVRKCIKKDSGKEFAAKFMRKRRKGQDCRMEI IHEIAVLELAQDNPW  
VINLHEVYETASEMILVLEYAAGGEIFDQCVADREEAFKEKDVQRLMRQILEGVHFLHTR  
DVVHLDLKPQNILLTSESPLGDIKIVDFGLSRILKNSEELREIMGTPEYVAPEILSYDPI  
SMATDMWSIGVLTYVMLTGISPFLGNDKQETFLNISQMNLSYSEEFVDVLSAVDFIRT  
LLVKKPEDRATAEECLKHPWLTQSSIQEPSFRMEKALEEANALQEGHSVPEINSDDTKSE  
TEESIVTEELIVTSTYTLGQCRQSEKEKMEQKAI SKRFKFEEPLLQEI PGFIY

SEQ ID NO: 152\_AA021445\_H  
MPARIGYYEIDRTIGKGNFAVVRATHLVTKAKVAIKIIDKTQLDEENLKKIFREVQIMK  
MLCHPHIIRLYQVMETERMIYLVTEYASGGEIFDHLVAHGRMAEKEARRKFKQIVTAVYF  
CHCRNIVHRDLKAENLLLDANLNKIADFGFSNLFTPGQLLKTWCGSPPYAAPELFEGKE  
YDGPVKDIWSLGVVLYVLVCGALPFDGSTLQNLRARVLSGKFRI PPFMSTECEHLIRHML  
VLDPNKRLSMEQICKHKWMKLGADPNFDRLIAECQQLKEERQVDPLNEDVLLAMEDMGL  
DKEQTLQSLRSDAYDHYSAIYSLCDRHKRHKTLRLGALPSMPRALAFQAPVNIQAEQAG  
TAMNISVPQVQLINPENQIVEPDGTLNLDSDGEGEPSPEALVRYLSMRRHTVGVADPRTE  
VMEDLQKLLPGFPGVNPQAPFLQVAPNVNFMHNLPMQNLOPTGQLEYKEQSLLOPPTLQ  
LLNGMGPLGRRASDGGANIQLHAQQLLKRPRGSPPLVTMTPAVPAVTPVDEESSDGEPDQ  
EAVQRYLANRSKRHTLAMTNPTAEIPDLQRLQGGQPPFRSRVWPHLVDPQHRSTYKDSN  
TLHLPTERFSPVRRFSDGAASIQAFAHLEKMGNNSSIKQLQCECEQLQKMYGGQIDERT  
LEKTQQQHMLYQQEQHHQILQQQIQDSICPPQPSPLQAACENQPALLTHQLQRLRIQPS  
SPPNHPNNHLFRQPSNSPPPMSSAMIQPHGAASSSQFQGLPSRSAIFQQQPENCSPPN  
VALTCLGMQQPAQSQQVTIQVQEPVDMLSNMPGTAAGSSSGRGISISPSAGQMOMQHRTNL  
MATLSYGHRPLSKQLSADSAEAHSLNVNRFSPANYPDQAHLPFLFSDQSRGSPSSYSPST  
GVGFSPTQALKVPPLDQFPTFPFSAHQPPHYTTALQQAALLSPTPPDYTRHQQVPHILO  
GLLSPRHSLTGHSIDIRLPPTFAQLIKRQQQQRQQQQQQQQQEQEYQELFRHMNQGDAGSL  
APSLGGQSMTERQALSQNADSYHHHTSPQHLLQIRAQECVSQASSPTPPHGYAHQPALM  
HSESMEEDCSCEGAKDGFQDSKSSSTLTGCHDSPLLLSTGGPGDPESLLGTVSHAQELG  
IHPYGHQPTAAFSKNKVPSREPVIGNCMDRSSPGQAVELPDHNLGLYPARPSVHEHHRPR  
ALQRHHTIQNSDDAYVQLDNLPGMSLVAGKALSSARMSDAVLSQSSLMGSSQQFQDGENEE  
CGASLGGHEHPDLSDGSQHLNSSCYPSTCITDILLSYKHPEVSFSMEQAGV

SEQ ID NO: 153\_2R22-5-11\_H  
MTAVYMNGGGLVNPHYARWDRRDSVESGCQTESSKEGEGQPRQLTPFEKLTQDMSQDEK  
VVREITLGKRIGFYRIRGEIGSGNFSQVKLGIHSLTKEKVAIKILDKTCLDQKTQRLLSR  
EISSMEKLHHPNIIRLYEVVETLSKLHLVMEYAGGELFGKISTEGKLSEPESKLIFSQI  
VSAVKHMHENQI IHRDLKAENVFYTSNTCVKVGDFGFSTVSKKGEMLNTFCGSPPYAAPE

## FIGURE 1H

LFRDEHYIGIYVDI WALGVLLYFMVTGTMPFRAETVAKLKKSILEGTYSVPPHVSEPCHR  
 LIRGVLLQIPTERYGIDCIMNDEWMQGVPTPLEPFQLDPKHLSETSTLKEEENEVKST  
 LEHLGITEEHIRNNQGRDARSSITGVYRIILHRVQRKKALESVPVMMLPDPKERDLKKGS  
 RVYRGIRHTSKFCSIL

SEQ ID NO: 154\_R31237\_1\_H, AAC33487  
 MSTRTPLPVTNERDTENHTSHGDGRQEVTSRTSRSGARCRNSIASCADQPHIGNYRLLK  
 TIGKGNFAKVKLARHILTGREVAIKI IDKTQLNPTSLQKLFREVRIMKILNHPNIVKLFE  
 VIETEKTLYLIMEYASGGEVFDYLVAHGRMKEKEARSKFRQIVSAVQYCHQKRIVHRDLK  
 AENLLLDADMNIKIADFGFSNEFTVGGKLDTFGSGPPYAAPELFQGGKYDGPVDVWSLG  
 VILYTLVSGSLPFDGQNLKELRERVLRGKYRIPFYMSTDCENLLKRFLVLNPIKRGTLQ  
 IMKDRWINAGHEEDELKPFVEPELDISDQKRIDIMVGMGYSQEEIQESLSKMKYDEITAT  
 YLLGRKSSSELDASDSSSSSNLSLAKVRPSSDLNNSTGQSPHHKVQSVSSSQKQRRYS  
 HAGPAIPSVVAYPKRSQTSTADGDLKEDGISSRKSSGSAVGGKGIAPASPMGNASNPKN  
 ADIPERKKSSTVPSSNTASGGMTRNTYVCSERTTADRHSVIQNGKENSTIPDQRTPVAS  
 THSISSAATPDRI RFPRGTASRSTFHGQPRERRATYNGPPASPSLSHEATPLSQTRSRG  
 STNLFSLKTSKLTRSRNVSAEQKDENEAKPRSLRFTWSMKTSSMDPGDMMREIRKVL  
 ANNCDYEQRRERFLFCVHGDGHAENLVQWEMEVCCLPRLSLNGVRFKRISGTSIAFKNIA  
 SKIANELKL

SEQ ID NO: 155\_W90839\_M  
 KGPSWSSRSLGARCRNSIASCPEEQPHVGNRYLLRTIGKGNFAKVKLARHILTGREVAIK  
 IIDKTQLNPSSLQKLFREVRIMKGLNHPNIVKLFEVIETEKTLYLMYASAGEVFDYLV  
 SHGRMKEKEARAKFRQIVSAVHYCHQKNIVHRDLKAENLLLDAAENIKIADFGFSNEFTL  
 GSKLDTFGSGPPYAAPELFQGGKYDGPVDIWSLGVIYTLVSGSLPFDGHNKELRERV  
 LRGKYRVPFYMSTDCESILRRFLVLNPAKRCLEQIMKDKWINIGYEELKPDTELKEE  
 RMPGRKASCSAVGSGSRGLPPSSPMVSSAHNPNAEI PERRKDSTSTPNLPPSMMTRN  
 TYVCTERPGSERPSLLPNGKENSSTSRVPPASPSHSLAPPSGERSRLARGSTIRSTFH  
 GGQVRDRRAGSGSGGVQNGPPASPTLAHEAAPLPSGRPRPTTNLFTKLTSLTRRVTD  
 PERIGGPEVTSCHLPWDKTETAPRLLRFPWSVKLTSSRPS

SEQ ID NO: 156\_406786.5\_H  
 MEVGGLTVFEEDQRCLSQSLPLPVSAEGPAAQTAEPSRSFSSAHRHLSRRNGLSRLCQS  
 RTALSEDRWSSYCLSSLAQNICSTKLHCPAAPEHTDPSEPRGSVSCCSLLRGLSSGWSS  
 PLLPAPVCNPNKAI FTVDAKTTEILVANDKACGLLGYSQDLIGQKLTQFFLRSDSDVVE  
 ALSEEHMEADGHA AVVFGTVVDI ITRSGEKI PVSVMKMRQERRLCVVLPEPVERVST  
 WVAFQSDGTITSCDSLFAHLHGYSVEDVAGQHITDLIPSVQLPPSGQHIPKNLKIQRSV  
 GRARDGTTFFLSLKLKSQPSSEEATTGEAAPVSGYRASVWVFCTISGLITLLPDGTIHGI  
 NHSFALTFLGYGKTELLGKNITFLIPGFYSYMDLAYNSSLQLPDLASCLDVGNESGGER  
 TLDPWQGGQDPAEGGQDPRINVVLGGHVVPDEIRKLMEQDIFTGTQTELIAGGQLLSC  
 LSPQAPAGVDNVEGSLPVHGEQALPKDQOITAGREEPVAI ESPGQDLLGESRSEPVDV  
 KPFAECEDSEAPVPAEDGGSDAGMCLCQKAQLERMVSGSGSLWAGAAVAKPQAKGQ  
 LAGGSLLMHCPCYGSEWGLWWSQDLAPSPSGMAGLSFGTPTLDEPWLGVENDREELQTC  
 LIKEQLSQLSLAGALDVPHAEVPTCEQAVTAPVSSCDLGGRDLCGGCTGSSSACYALAT  
 DLPGGLEAVEAQEVDVNSFSWNKELFFSDQTDQTSNCS CATSELRETPSSSLAVGSDPD  
 VGSLEQEGSCVLDRELLLTGTCDVLDGQRRFRESCVGHDPTEPLEVCLVSSEHYAASD  
 RESPGHVPSTLDAGPEDTCPSAEPRNLNVQVTSTPVI VMRGAAGLQREIQEGAYSGSCYH  
 RDGLRLSIQFEVRRVELQGPTPLFCCWLVDLLHSQRDSAARTLFLASLPGSTHSTAAE  
 LTGPSSLVEVLRRPWFEEPPKAVELEGLAACGEYSQKYSTMSPLGSGAFGFVWTAVDKG  
 KNKEVVVKFIKKEKVLDCWIEDPKLGKVTLEIAILSRVEHANI I KVLDFENQGFQFLV

## FIGURE 11

MEKHGSGLDLFAFIDRHPRLDEPLASYIFRQVRAGQSRLVSAVGYLRLKDIHRDIKDEN  
 IVIAEDFTIKLIDFGSAAYLERGKLFYTCGTIEYCAPEVLMGNPYRGPELEMWSLGVTL  
 YTLVFEENPFCELEETVEAAIHPPYLVSKEMLSVSGLLQPVPERRTTLEKLVTDWPVTQ  
 PVNLADYTWEVFRVKNKPESGVLSAASLEMGNRSLSDVAQAQELCGGPVPGEPNGQGCL  
 HPGDPRLLTS

SEQ ID NO: 157\_AA544838\_M 406786\_M  
 TRPHPCLDPLASFIFRQLVSAVGYLHSQGIHRDIKDENVIAEDFTIKLIDFGSAAYL  
 ERGKLFYTCGTIEYCAPEVLIGNPYRGPELEMWSLGVTLTYTLIFEENPFCEVEETMEAV  
 IHPPFLVSQELMSLLSGLLQPCPEQRTTLEKLIRDPWVTQPVNLASYTWEVCRNTNPES  
 GLLSAASLEIGSRSPSEMAQREGLCGPPAPRETRGDQHCLHLKDPSLPVS

SEQ ID NO: 158\_AA785735\_H  
 MVMADGPRHLQRGPPVRVGFYDIEGTLGKGNFAVVKLGRHRITKTEVAIKIIDKSQLDVN  
 LEKIYREVQIMKMLDHPHIKLYQVMETKSMYLVTEYAKNGEIDYLANHGRLNESEAR  
 RKFWQILSAVDYCHGRKIVHRDLKAENLLDNNMNIKIADFGFGNFFKSGELLATWCGSP  
 PYAAPEVFEGQQYEGPQLDIWSMGVVLYVLVCGALPFDGPTLPILRQRVLEGRFRIPIYFM  
 SEDCEHLIRMLVLDPSKRLTIAQIKEHKWMLIEVPVQRPVLYPQEQENEPSIGEFNEQV  
 LRLMHSGLIDQQKXIESLQNKSYNHFAAIYFLLVERLKSRRSSFPVEQRLDGRQRRPSTI  
 AEQTVAKAQTVGLPVTMHSNMRLLRSALLPQASNVEAFSFPASGCQAEAAFMEEECVDT  
 PKVNGCLLDPPVPLVRKGCQSLPSNMMETSIDEGLETEGEAEEDPAHAFAEFQSTRSGQ  
 RRHTLSEVTNQLVVMGAGKIFSMNDSPLSDVDSEYDMGSVQORDLNFLDNPSLKDIML  
 ANQPSPRMTSPFISLRPTNPAMQALSSQKREVNHRSPVSFREGRRASDTSLTQGI VAFRO  
 HLQNLARTKGILELNKVQLLYEQIGPEADPNLAPAAPQLQDLASSCPQEEVSQQQESVST  
 LPASVHPQLSPRQSLETQYLQHRLOKPSLLSKAQNCTQLYCKEPPRSLEQQQLQEHRLQOK  
 RLFLQKQSQLQAYFNQMQIAESSYPQPSQQLPLPRQETPPPSQQAPPFSLTQPLSPVLEP  
 SSEQMQYSPFLSQYQEMQLQPLPSTSGPRAAPPLPTQLQQQQPPPPPPPPPPRPGAAPA  
 PLQFSYQTCELPSAASPAPDYPTPCQYPVDGAQQSDLTGPDCPRSPGLQEAPSSYDPLAL  
 SELPGLFDCEMLDAVDPQHNGYVLVN

SEQ ID NO: 159\_AA207220\_H  
 MESLVFARRSGPTPSAAELARPLAEGLIKSPKPLMKKQAVKRHHHKHNLRRHYEFLETLG  
 KGTYGKVKKARESSGRLVAIKSIRKDKIKDEQDLMHIRREIEIMSSLNHPHIIAIEHVFE  
 NSSKIVIMEYASRGDLYDIISERQQLSEREARHFFRQIVSAVHYCHQNRVVRDLKLEN  
 ILLDANGNIKIADFGLSNLYHQGKFLQTFCSPLYASPEIVNGKPYTGPEVDSWSLGVLL  
 YILVHGTMPFDGHDHKILVKQISNGAYREPPKPSDCLXGLIRWLLMVNPTRRATLEDVAS  
 HWWVNWGYATRVGEQAPHEGGHPGSDSARASMDWLRSSRPLENGAKVCSFFKQHAP  
 GGGSTTPGLERQHSLKSRKENDMAQSLHSDTADDTAHRPGKSNLKLKPKGILKKKVSASA  
 EGVQEDPPELSPIPASPGQAAPLLPKKGILKKPRQRESGYYSSEPPSESSELLDAGDVFV  
 SGDPKEQKPPQASGLLLHRKGILKLNGKFSQTALELAAPTTFGSLDELAPPRPLARSRP  
 SGAVSEDSILSSESFDQLDLPERLPEPPLRGCVSDNLTGLEPPSEGGSGCLRRWRQDP  
 LGDSCFSLTDCQEVATATYRQALRVCSKLT

SEQ ID NO: 160\_AA426580\_H, MAK\_V\_H  
 MPAAAGDGLLGEPAAPGGGGGAEDAARPAACEGSFLPAWVSGVPRERLRDFQHHKRVGN  
 YLIGSRKLGEFSFAKVREGLHVLTGEKVAIKVIDKKRAKDTYVTKNLRRREGQIQQMIRH  
 PNITQLLDILETENSYYLMELCPGGNLMHKIYEKKRLEESEARRYIRQLISAVEHLHRA  
 GVVHRDLKIEENLLDEDNNIKLIDFGLSNCAGILGYSDPFSTQCGSPAYAAPELLARKKY  
 GPKIDVWSIGVNMAMLTGTLPTVEPFSRLALYQKMDKEMNPLPTQLSTGAISFLRSL  
 LEPDPVKRPNIQQALANRWLNENYTGKVP CNVTYPNRI SLEDLSPSVVLHMTKLGKYN



## FIGURE 1J

DVINTVLSNRACHILAIYFLLNKKLERYLSGKSDIQDSLKYKTRLYQIEKYRAPKESYEA  
 SLDTWTRDLEFHAVQDKKPKKEQKRGDFLHRPFSKKLDKNLPSHKQPSGSLMTQIQNTKA  
 LLKDRKASKSSFPDKDSFGCRNIFRKTSDSNCVASSSMEFIPVPPPRTPRIVKKPEPHQP  
 GPGSTGIPHKEDPLMLDMVRSFESVDRDDHVEVLSPSHHYRILNSPVSLARRNSSERTLS  
 PGLPSGMSPLHTPLHPTLVSFHEDKNSPPKEEGLCCPPVPSNGPMQPLGSPNCVKSR  
 GRFPMMGIGQMLRKRHQSLOPSADRPLEASLPPLQPLAPVNLAFLDMADGVKTQC

SEQ ID NO: 161\_Z36720\_H

MDTKLNMLNEKVDQLLHFQEDVTEKLQSMCRDMGHLERGLHRLEASRAPGPGGADGVPHI  
 DTQAGWPEVLELVRAMQQDAAQHGARLEALFRMVAADVRAIALVGATFQKSKVADFLMQG  
 RVPWRRGSPGDSPEEWVKEEEVCFMPPVPPAPGAAGQSLQKDKGELSAEQGIWATLMTLV  
 IMVTAANKERVEEEGGKPKHVLSTSGVQSDAREPGEESQKADVLEGTAERLPPIRASGLG  
 ADPAQAVVSPGQGDGVPGPAQAFPGHLPLPTKVEAKAPETPSENLRTGLELAPAPGRVNV  
 VSPSLEVAPGAGQGASSSRPDPEPLEEGTRLTPGPGPQCPCPPGLPAQARATHSGGETPP  
 RAALLKGAVAPGFSRRDLVFPSIFCACLGISIHQEMDTPGEMLMTGRGSLGPTLTTEAP  
 AAAQPGKQGGPGTGRCLQAPGTEPGEQTPEGARELSPLQESSSPGGVKAEEEQRAGAEPG  
 TRPSLARSDNDHEVGALGLQQGKSPGAGNPEPEQDCAARAPVRAEAVRRMPPGAEGSV  
 VLDDSPAPPAPFEHRVSVKETSISAGYEVQCQHEVLGGGRFGQVHRCTEKSTGLPLAAKI  
 IKVKSADREDVKNEINIMNQLSHVNLIQLYDAFESKHSCTLVMEYVDGGELFDRIITDEK  
 YHLTELDVVLFTROIPEGVHYLHQHYILHLDLKPENILCVNQTGHQIKIIDFGLARRYKP  
 REKLKVNFGTPEFLAPEVVNYEFVSFPTDMWSVGIVITYMLLSGLSPFLGETDAETMNFIV  
 NCSWDFDADTFEGLSEEAKDFVSRLLVKEKSCRMSATQCLKHEWLNLPKASRSKTRLK  
 SQLLLQKYIAQRKWKKHFFYVVTAAANRLRKFTSP

SEQ ID NO: 162\_SGK088\_H

GEMALFECLVAGPTDVEVDWLCRGRLLQPALLKCKMHFDGRKCKLLLTSVHEDDSGVYTC  
 KLSTAKDELTCARLTVRPSLAPLFTRLLEDVEVLEGRAARFDCKISGTPPPVVTWTHFG  
 CPMEESENLRLRQDGLHSLHIAHVGSEDEGLYAVSAVNTHGQAHCSAQLYVEEPRTAAS  
 GPSSKLEKMPPIPEEPEQGELERLSIPDFLRPLQDLEVGLAKEAMLECQVTGLPYPTISW  
 FHNGHRIQSSDDRRMTQYRDVHRLVFPVAVGPQHAGVYKSVIANKLGAACYAHLYVTDVV  
 PGPPDGAPQVVAVTGRMVTLTWNPPRSLDMAIDPDSLTYTVQHQLVGLSDQWTALVTGLRE  
 PGWAATGLRKGVQHIFRVLSTTVKSSSKPSPSEPVLLEHGPTLEEAPAMLDKPDIVYV  
 VEGQPASVTVTFNHVEAQVWVRSCRGALLEARAGVYELSQPDDDOYCLRICRVSRDMGA  
 LTCTARNRHGTQTCVSTLELAEAPRFESIMEDVEVGAGETARFAVVVEGKPLPDIMWYKD  
 EVLLTESSHVSFVYEENECSLVVLSTGAQDGGVYTCTAQNLAGEVSCAELAVHSAQTAM  
 EVEGVGEDEDHRGRRLSDFYDIHQEIGRGAFSYLRRIVERSSGLEFAAKFIPSQAKPKAS  
 ARREARLLARLQHDCVLYFHEAFERRRGLVIVTELCTEELLERIARKPTVCESEIRAYMR  
 QVLEGIHYLHQSHVLHLDVKPENLLVWDGAAGEQQVRI CDFGNAQELTPGEPQYCQYGTP  
 EFVAPEIVNQSPVSGVTDIWPVGVVAFCLTGISPFVGENDRITLMNIRNYNVAFEETTF  
 LSLSREARGFLIKVLVQDRLRPTAEETLEHPWFKTQAKGAEVSTDHLKFLSRRRWQRSQ  
 ISYKCHLVLRPIPELLRAPPERVWVTMPRRPPPSGGLSSSSDSEEELEELPSVPRPLQP  
 EFGSRVSLTDIPTEDALGTPETGAATPMDWQEQGRAPSQDQEAPEALPSPGQEPAA  
 GASPRRGELRRGSSAESALPRAGPRELGRGLHKAASVELPQRRSPGPGATRLARGGLGEG  
 EYAQRLQALRQRLLRGGPEDGKVSGLRGPLLESGLGRARDPRMARAASSEAAPHHQPPL  
 NRGLQKSSSFSGQEAEPGRHRRAGAPLEIPVARLGARRLQESPSLSALSEAQPSPARP  
 SAPKPSTPKSAEPSATTPSDAQPPAPQPAQDKAPEPRPEPVRASKPAPPPQALQTLALP  
 LTPYAQIIQSLQLSGHAQGPSQGPAAAPPSEPKPHAAVFARVASPPPGAPEKRVPSAGGPP  
 VLAEKARVPTVPPRPGSSSLSSSIENLESEAVFEAKFKRSRESPLSLGLRLLSRSRSEERG  
 PFRGAEEEDGIYRPSAGTPLELVRRPERSRSVQDLRAVGEPGLVRRLLSLSLSQRLRRT  
 PAQRHPAWEARGGDGESSEGGSSARGSPVLAMRRRLSFTLERLSSRLQRSGSSSEDSSGAS



## FIGURE 1K

GRSTPLFGRLRRATSEGESLRRRLGLPHNQLAAQAGATTTPSAESLGSEASATSGSSAPGES  
 RSRLRWGFSRPRKDKGLSPPNLSASVQEELGHQYVRSESDFPVVFHIKLKDQVLLGEAA  
 TLLCLPAACPAPHISWMKDKSLRSEPSVIVSCKDGRQLLSIPRAGKRHAGLYECSATN  
 VLGSITSSCTVAVARVPGKLAPPEVTQTYQDTALVLWKPGDSRAPCTYTLERRVDGESVW  
 HPVSSGIPDCYYNVTHLPVGVTVRFRVACANRAGQGPFSSNSSEKVFVRGTQDSSAVPSAA  
 HQEAPVTSRPARARPPDSPTSLAPPLAPAAPTPPSVTVSPSSPPTPPSQALSSLKAVGPP  
 PQTTPRRHRGLQAARPAEPTLPSTHVTTPSEP KPFVLDGTPI PASTPQGVKPVSSSTPVY  
 VVTSFVSAPPAPEPPAPEPPPEPTKVTVQSLSPAKEVVSSPGSSPRSSPRPEGTTLRQGP  
 PQKPYTFLEEKARGFRGVVRACRENATGRTFVAKIVPYAAEGKPRVLQEYEVRLTLHHER  
 IMSLHEAYITPRYLVLIAESCGNRELLCGLSDRFYSEDDVATYMVQLLQGLDYHLGHV  
 LHLDIKPDNLLAPDNALKIVDFGSAQYPNPQALRPLGHRTGTLEFMAPEMVKGEPIGSA  
 TDIWGAGVLTYYIMLSGRSPFYEPDPQETEARIVGGRFADFQLYPNTSQSATLFLRKVLSV  
 HPWSRPSLQDCLAHPWLQDAYLMKLRRQTLTFTTNRLKEFLGEQRRRRAEAAATRHKVLLR  
 SYPGGP

SEQ ID NO: 163\_AA542015\_M SGK088\_M  
 ATDIWGAGVLTYYIMLSGYSPFYEPDPQETEARIVGGRFADFQLYPNTSQSATLFLRKVLS  
 VHPWSRPSLQDCLAHPWLQDAYLMKLRRQTLTFTTNRLKEFLGEQRRRRAEAAATRHKVLL  
 RSYPGSP

SEQ ID NO: 164\_R19772\_H  
 MKGGDRAYTRGPSLGLWFAKCCCCFPCRDAYS HSSSENGGKSES VANLQAQPSLNFIHSS  
 PGPKRSTNTLKKWLTSPVRRNLNSGKADGNIKKQKKVRDGRKSF DLGSPKPGDETT PQGDS  
 ADESKKGWGEDEPDEESHTPLPPMKIFDNDPTQDEMSSSLAARQASTEVP TAADLVNA  
 IEKLVKNKLSLEGSSYRGS LKDPAGCLNEGMAPPTPPKNPEEEQKAKALGRMFVNL ELV  
 QTEKDYVKDLGIVVEGFMKRIEEKGVPEDMRGKDKIVFGNIHQIYDWHKDFFLAELEKCI  
 QEQRDLAQLFIKHERKLHIYVWYQNKPRSEYIVAEYDAYFEEVKQEINQRLTSLDFLIK  
 PIQRITKYQLLLKDFLRYSEKAGLECS D IEKAVELMCLVPKRCNDMMNLGR LQGFEGT LT  
 AQGKLLQQDTFYVIELDAGMQSRTKERRVFLFEQIVIFSELLRKGS LTPGYMFKRSI KMN  
 YLVLEENVNDNDPCKFALMNRETSE RVVLQAANADIQQAWVQDINQVLETQRDFLNALQSP  
 IEYQRKERSTAVMRSQPARLPQASPRPYSSVPAGSEKPPKGSSYNPPLPPLKISTSN GSP  
 GFEYHQPGDKFEASKNDLGGCNGTSSMAVIKDYYALKENEICVSQGEVVQVLAVNQQNM C  
 LVYQPASDHSPAAEGWVPGSILAPLTKATAAESDGSIKKSCSWHTLRMRKRAEVENTGK  
 NEATGPRPKDILGNKVS VKETNSSESECDLDPNTSMEILNPNFIQEVAP EFLVPLVD  
 VTCLLGDTVILQCKVCGRPKPTITWKGPDQNI LDTDNSSATYTVSSCDSGEITLKI CNLM  
 PQDSGIYTCIATNDHGTTSATVKVQGVPAAPNRPIAQERSCTSVILRWLPPSSTGNCT  
 ISGYTVEYREEGSQIWQQSVASTLD TYLVIDLSPGCPYQFRVSASNPWGISLPSE PSEF  
 VRLPEYDAAADGATISWKENFDSAYTELNEIGRGRFSIVKKCIHKATR KDVAVKFVNKKM  
 KKKEQAAHEAALLQHLQHPQYITLHDTYESPTS YILILELMDDGRLLDYLMNHDELME EK  
 VAFYIRDIMEALQYLHNCRV AHLDIKPENLLIDLRI PVPRVKLIDLEDAVQISGHFHIH H  
 LLGNPEFAAPEVIQGI PVSLGTDIWSIGVLT YVMLSGVSPFLDESKEETCINVC RVDFS F  
 PHEYFCGVSN AARDFINVILQEDFRRRPTAATCLQHPWLQPHNGSYSKIPLDTSRLACFI  
 ERRKHQNDVRPIPNVKS YIVNRVNQGT

SEQ ID NO: 165\_5R72\_8\_2\_H  
 MADSGLDKKSTKCPDCSSASQKDVLCVCSSKTRVPPVLV VEMSQTSSIGSAESLISLERK  
 KEKNINRDITSRKDLPSRTSNVERKASQQQWGRGNFTEGKVPHIRIENGAAIEEIYTFGR  
 ILGKGSFGIVIEATDKETETKWA I KKVNKEKAGSSAVKLLEREVNILKSVKHEHIHLEQ  
 VFETPKMYLVMELCEDGELKEILDRKGHFSENETRWIIQSLASAIAYLHNNDIVHRDLK  
 LENIMVKSS LIDNNEINLNIKVTD FGLAVKKQSRSEAMLOATCGTPIYMAPEVISAHDY

## FIGURE 1L

SQQCDIWSIGVVMYMLLRGEPPFLASSEAKLFELIRKGE LHFENAVWNSISDCAKSVLKQ  
 LMKVDPAHRI TAKELLDNQWLTGNKLSSVRPTNVLEMMKEWKNNPESVEENTTEENKPKS  
 TEEKLSYQPWGNVPETNYTSDEEEEEKQSTAYEKQFPATSKDNFDMCSSSFTSSKLLPAE  
 IKGEMEKTPVTPSQGTATKYPAKSGALSRTKKKL

SEQ ID NO: 166\_SGK309\_H

MQCLAAALKDETNMSGGGEQADILPANYVVKDRWKVLKKIGGGGFGEIYEAMDLLTREN  
 ALKVESAQQPKQVLKMEVAVLKKLQGSGLGQGDGKEEMMKPGAKRGKDHVCRFIGCGRNE  
 KFNYYVMQLQGRNLADLRRSQPRGFTTLSTTLRLGKQILESIEAIHSVGLHRDIKPSNF  
 AMGRLPSTYRKCYMLDFGLARQYTNNTGDVRPPRN VAGFRGTVRYASVNAHKNREMGRHD  
 DLWSLFYMLVEFAVGQLPWRKIKDKEQVGMKEKEYEHRMLLKHMPSEFHLFLDHIASLDY  
 FTKPDYQLIMSVFENSMKERGIAENAFDWEKAGTDALLSTSTSTPPPAEHPADGSHVWG  
 GQCDASAWGPAPGEHRGCATGRAPEXPGECTPNSAREALXGAGPQSPPCPPRGSXGXSL  
 GGDRCQPEQTPDQHRQSNCRQGEGRGWPFLLSPPIPSLVPLPCSSXAPCPPPISLLARPLF  
 PVPSPALASLCLPSSSSSVSFTLRRPSA

SEQ ID NO: 167\_AA234451\_H

MSGGGEQLDILSVGILVKERWKVLRKIGGGGFGEIYDALDMLTRENVALKVESAQQPKQV  
 LKMEVAVLKKLQGDHVCRFICGGRNDRFNYYVMQLQGRNLADLRRSQSRGTFTISTTLR  
 LGRQILESIESIHSVGSXHRDIKPSNFMGRFPSTCRKCYMLDFGLARQFTNSCGDVRPP  
 RAVAGFRGTVRYASINAHNRNEMGRHDDLWSLFYMLVEFVVGQLPWRKIKDKEQVGSIKE  
 RYDHRMLMLKHLPPFEFSIFLDHISSLDYFTKPDYQLLTSVFDNSIKTFGVIESDPFDWEKT  
 GNDGSLTTTTTTSTTPQLHTRLTPAAIGIANATPIPGDLLRENTDEVFPDEQLSDGENGIP  
 VGVSPDKLPGSLGHPRPQEKDVWEEMDANKNKIKLGICKAATEEENSHGQANGLLNAPSL  
 GSPIRVRSEITQPDRIPLVRKLRSIHSFELEKRLTLEPKPDTDKFLETWYKIVYFSF

SEQ ID NO: 168\_AA435956\_H

TFTIFFEMTVFDLEAKSARGGSNLLMDSVSSFQLFMFQLLRGLAYIHHQHVLHRDLKPQN  
 LLISHLGELKLADFLARAKSIPSQTYSSVVTLWYRPPDALLGATEYSSSELDIWAGCI  
 FIEMFQQQPLFPGVSNILEQLEKIWEVLGVPTEDTWPGVSKLPNYPWFPLPTPRSLHV  
 VWNRLGRVPEAEDLASQMLKGFPRDRVSAQEALVHDYFSALPSQLYQLPDEESLFTVSGV  
 RLKPEMCDLLASYQKGHHPAQFSKCW

SEQ ID NO: 169\_AA626859\_H

NGVADGVIKSVLWQTLQALNFCHIHNCIHRDIKPENILITKQGIKICDFGFAQILIPGD  
 AYTDYVATRWYRAPELLVGDTQYGSVVDIWAIGCVFAELLTGQPLWPGKSDVDQLYLIIR  
 TLGKLI PRHQSI FKSNGFFHGISIPEPEDMETLEEKFSVHPVALNFMKGCLKMNPDRL  
 TCSQLLESSYFDSFQEAQIKRKARNEGRNRRRQQNQLLPLIPGSHISPTPDGRKQVLQLK  
 FDHLPNI

SEQ ID NO: 170\_AA061797\_M

KIALREIRMLKLKHPNLVNLIEVFRKRKMHLVFEYCDHTLLNELERNPNGVSDGVIKSV  
 LWQTLQALNFCHKHNCIHRDVKPENILITKQGMKICDFGFARILIPGDAYTDYVATRWY  
 RAPELLVGDTKYGSVVDVWAVGCVFAELLTGQPLWPGKSDVDQLYLIIRTLGKLI PRHQ  
 IFRSNQFFRGISIPEDMETLEEKFSNVQPVALSFMKGCLKMNPDRLTCAQLLDSAYF  
 ESFQEDQMKRKARSEGRSRRRQQNQLLPLIPGSHISPTPDGRKQVVQLKFDHLPNI

SEQ ID NO: 171\_AA397553\_H

MPNSERHGGKKDGSGGASGTLQPSSGGGSSNSRERHRLVSKHKRHSKHSKMDGLVTPEA  
 ASLGTVIKPLVEYDDISSDSTFSDDMAFKLDRRENDERRGSDRSRLHKKRHHQHRRSR

## FIGURE 1M

DLLKAKQTEKEKSQEVSSKSGSMKDRI SGSSKRSNEETDDYGKAQVAKSSSKESRSSLH  
 KEKTRKERELKSGHKDRSKSHRKRETPKSYKTVDSPKRRSRSPHRKWSOSSKQDDSPSGA  
 SYGQDYDLSPSRSTSSNYDSYKKS PGSTSRRQSVSPPYKEPSAYQSSTRSPSPYRRQR  
 SVSPYSRRRSSSYERSGSYSGRSPSPYGRRRSSSPFLSKRSLRSPLPSRKSMKSRSRSP  
 AYSRHSSSHSKKKRSSSRHSSI SPVRLPLNSSLGAELSRKKKRAAAAAAKMDGKES  
 KGSPVFLPRKENSSVEAKDSGLESKKLPRSVKLEKSAPDTELNVNTHLNTTEVKNSSDTGK  
 VKLDENSEKHLVKDLKAQGTDRDSKPIALKEEIVTPKETETSEKETPPPLPTIASPPPLP  
 TTTPPPQTPLPLPLPIPALPQQPPLPPSQPAFSQVPASSTSTLPPSTHSTSAVSSQAN  
 SQPPVQVSVKTQVSVTAAPHLKTSTLPLPLPLPLPGDDMDSPKETLPSKPVKKEKEQ  
 RTRHLLTDLPLPELPGDLSPPDSPEPKAITPPQQPYKKRPKICCPRYGERRQTESDWG  
 KRCVDKFDIIGIIGEGTYGQVYKARDKDTGELVALKKVRLDNEKEGFPITAIKILRQ  
 LIHRSVNMKEIVTDKQDALDFKKDKGAFYLVFEYMDHDLMLLESGLVHFSEDHIKFSM  
 KQLMEGLEYCHKKNFLHRDIKCSNILLNNSGOIKLADFGLARLYNSEESRPYTNKVITLW  
 YRPELLLGEERYTPAIDVWSCGICLGELFTKKPIFQANLELAQLELISRLCGSPCPAVW  
 PDVIKLPYFNTMKPKKQYRRRLREEFSFIPSAALDLLDHMLTLDPSKRCTAEQTLQSDFL  
 KDVELSKMAPDPLPHWQDCHELWSKKRRRQSQSVVVEEPPPSKTSRKETTSGTSTEPVK  
 NSSPAPPQAPAGKVESGAGDAIGLADITQQLNQSELAVLLNLLQSQTDLSIPQMAQLNI  
 HSNPEMQQLEALNQSISALTEATSQQQDSETMAPEESLKEAPSAPVILPSAEQMTLEAS  
 STPADMQNILAVLLSQLMKTQEPAGSLEENNSDKNSGPQGPRRTPTMPQEEAAACPPHIL  
 PPEKRPPEPPPPPPPPPLVEGDLSAPQELNPAVTAALLQLLSQPEAEPPGHLPHHEH  
 QALRPMEYSTRPRPNRTYGNTDGPETGFS AIDTDERNSGPALTESLVQTLVKNRTFSGSL  
 SHLGESSSYQGTGSGVQFGDQDLRFARVPLALHPVVGQPFLLKAEGSSNSVVAETKLQNY  
 GELGPGTTGASSSGAGLHWGGPTQSSAYGKLYRGPTRVPPRGRGRGVY

SEQ ID NO: 172\_AA789239\_H  
 MEMYETLGKVGESYGTVMCKKHNTGQIVAIKIFYERPEQSVNKIAMREIKFLKQFHHE  
 NLVNLIEVFRQKKIHLVFEFIDHTVLDELQHYCHGLESKRRLKYLFIQLRAIDYLSNN  
 VIIHRDIKPENILVSQSGITKLCDFGFARTLAAPGDIYTDYVATRWYRAPELVLKDTSYG  
 KYVPVDI WALGCMIIEMATGNPYLPSSSDLDLLHKIVLKVXFMPPELKAKLLQEAKVNSLI  
 KPKESSKENELRKDERKTVYTNLLSSSVLGKEIEKEKKPKEIKVRVIVKVGGRGDI SEP  
 KKKEYEGGLGQDANENVHPMSPTKLVTIEPPNPINPSTNCNGLKENPHCGGSVTMPPI  
 NLTNSNLMAANLSSNLFHPSVRLTERAKKRTSSQSIGQVMPNSRQEDPGPIQSOMEKGI  
 FNERTGHSDQMANENKRKLNFSSDRKEFHFPPELPTIQSKDTKGMEVKQIKMLKRESKK  
 TESSKIPTLLNVDQNEKQEFIPLSLLSACCPIFTNICSQLTIRVEMAIARGRI

SEQ ID NO: 173\_AA124976\_M  
 LADIVHACLQIDPAERTSSTDLLRHDFYTRDGFIEKFIPELRAKLLQEAKVNSFIKPEN  
 FKENEPVRDEKKSFTNTLLYGNPSLYGKEVDKRAKELKVRVIAKAGGKGDVPDQKKP  
 EYEGDHRQQGTADDTQPSSLDKKPSVLELTNPLNPSSENSDGVKEDPHAGGCMIMPPINLT  
 SSNLLAANLSSNLSHPNSRLTERTKKRTSSQTIGOTLSNSRQEDTGPTQVQTEKGAFNE  
 RTGQNDQISSGNKRKLNF PKCDRKEFHFPPELPTVQAKEMKGMEVKQIKVLKRESKKTDS  
 SKIPTLLSMDPNQEKQEGGDGDCEGKNLKRNRFFFSR

SEQ ID NO: 174\_AA575635\_M CCRK\_M  
 SASGQLKIADFGLARVFS PDGGRLYTHQVATRWYRAPELLYGARQYDQGVLDWAVGCIMG  
 ELLNGSPLFPGENDIEQLCCVLRILGTPSPRVWPEITELPDYNKISFEEQAPVPLEEVL  
 DASPQALDLLGQFLLYPPRQRIASQALLHQYFFTAPLPAHPSELPIQRPGGPAPKAHP  
 GPPHVHDFHVDRPIEESLLNPELIRPFIPEG

## FIGURE 1N

SEQ ID NO: 175\_AA631990\_H  
 MITSISTEKSNGTHYPPMITTLQYYRGRGGKTAVVRHFS AEGPF AFAEMRHSKRTHCPDW  
 DSRESWGHE SYRGSHKRKRSHSSTQENRHCKPHHQFKESDCHYLEARSLNERDYDRRY  
 VDEYRNDYCEGYVPRHYHRDIESGYRIHCKSSVRSRRSSPKRKRNRHCSSHQSRSEIV  
 DTLGEGAFGKVVECIDHGMDGMHVAVKIVKNVGRYREARSEIQVLEHLNSTDPNSVFR  
 VQMLEWFDHHGHVCI VFELLGLSTYDFIKENSFLPFQIDHIRQMAYQICQSINFLHNNKL  
 THTDLKPENILFVKSDYVVKYNSKMKRDERTLKNNTDIKVVDFGSATYDDEHHSTLVSTRH  
 YRAPEVILALGWSQPCDVWSIGCILIEYYLGFTVFQTHDSKEHLAMMERILGPI PQHMIQ  
 KTRKRKYFHHNQLDWDEHSSAGRYVRRRCKPLKEFMLCHDEEHEKLFDLVRRMLEYDPTQ  
 RITLDEALQHPFFDLLKKK

SEQ ID NO: 176\_AA557536\_H  
 MCTVVDPRIVRRYLLRRQLGQGRTFREITLLQVSGLGPPVQSPCPGTDLSRQERNWPSWA  
 PEHSPSWPSSRLRLSPQEFGDHPNII SLLDVIRAENDRDIYLVFEFMDTDLNAVIRKGG  
 LQDVHVR SIFYQLLRATRFLHSGHVVRDQKPSNVLLDANCTVKLCDFGLARSLGDLPEG  
 PEDQAVTEYVATRWYRAPEVLLSSHRYTASCPRYTLGVDMWSLGCILGEMLRGRPLFPGT  
 STLHQLELILETIPPPSEEXRPRQTL DALLPPDTSPEALDLLRRLLVFAPDKRLSATQAL  
 QHPYVQRFHCP SDEWAREADVPRPRAHEGVQLSVPEYRSRVYQMI LECGSSGTSREKGP  
 GVSPSQAH LHKPRADPQLPSRTPVQGP RPQSSPGHDPAEHES PRAAKNVPRQNSAPLL  
 QTALLNGERPPGAKEAPPLTSLVKPSGRGAAPSLTSQAAAQVANQALIRGDWNRRGGV  
 RVASVQQVPPRLPPEARPGRRMFST SALQGAQGGARALLGGYSQAYGTVCHSALGHLPL  
 EGHV

SEQ ID NO: 177\_N28606\_H, MOK\_H  
 MKNYKAIGKIGEGTFSEVMKMQLRDGNYYACKQMKQRFESIEQVNNLREIQALRRLNPH  
 PNILMLHEVVFD RKSGSLALICELMDMNIYELIRGRYPLSEKKIMHYMYQLCKSLDHIH  
 RNGIFHRDV KPENILIKQDV LKLGDFGSCRSVYSKQPYTEYISTRWYRAPECLLTGDFYT  
 YKMDLWSAGCVFYEIASLQPLFPGVNELDQISKIHDVIGTPAQKILTKFKQSRAMNDFP  
 FKKGSGIPLLTNLS PQCLSLHAMVAYDPDERIAAHQALQHPYFQEQRKTEKRALGSHR  
 KAGFPEHPVAPEPLSNQCISKEGRKQKQSLKQEDRPKRRGPAYVMELPKLKLSGVVRL  
 SSYSSPTLQSVLGS GTNGRVPVLRPLKCI PASKKTD PQDLKPAPQQCRLPTIVRKGR

SEQ ID NO: 178\_AB023153\_H, ICK\_H  
 MNRYTTIRQLGDGT YGSVLLGRSIESGELIAIKMKRKFYSWEECMNQREVKSLKKNHA  
 NVVKLKEVIRENDHLYFIFEYMKENLYQLIKERNKLPESAIRNIMYQILQGLAFIHLK  
 FFHRDLKPENLLCMGP ELVKIADFG LAREIRSKPPYTDYVSTRWYRAPEVLLRSTNYSSP  
 IDVWAVGCIMAEVYTLRPLFP GASEIDTIFKICQVLGTPKKT DWPEGYQLSSAMNFRWPQ  
 CVPNNLKTLPNASSEAVQLLRDMLQWDPKKRPTASQALRYPYFQVGHPLGSTTQNLQDS  
 EKPQKGILERAGPPPYIKPVPPAQPPAKPHTRISSRQH QASQPPLHLTYPYKAEVSRTDH  
 PSHLQEDKPSPLLP SLHNKHPQSKITAGLEHKNGEIKPKSRRRWGLISRSTKDSDDWAD  
 LDDLDFSPSLSRIDLKNKKRQSDDTLCRFESVLDLKPSEPVG TGNSAPTQTSYQRRDTPT  
 LRSAAQHYLKH SRYLPGISIRNGILSNPGKEFIPPNPWSSSGLSGKSSGTMSVISKVNS  
 VGSSSTSSSGLTG NYVPSFLKKEIGSAMQRVHLAPIDPSPGYSSLKAMRPHPGRPFLDT  
 QPRSTPGLIPRPPAAQPVHGRTDWASKYPSRR

SEQ ID NO: 179\_AA839940\_M  
 SSNNGGMSAE EIGPGAEPMRGPSLATRDWRDET VGTDDLQGGIDPGAVSPEPGKDHA  
 GPGRTEAGRVSSAAEAAIVVLDDSAAPPAPFEHRVVS IKDTLISAGYTVSQHEVLGGGRF  
 GQVHRCTERSTGLALAAKIIKVKNVKDREDVKNEVNIMNQLSHVNLIQLYDAFESKNSFT  
 LIMEYVDGGELFD RITDEKYHLTEL DVVLFTRQICEGVHYLHQHYILHLDLKPENILCVS

## FIGURE 10

QTGHQIKIIDFGLARRYKPREKLKVNFGTPEFLAPEVVNYEFVSFPTDMWSVGVITYMLL  
 SGLSPFLGETDAETMNFIVNCSWDFDADTFKGLSEEAKDFVSRLLVKEKSCRMSATQCLK  
 HEWLNHLPAKASGSNVRLRSQQLLQKYMAQSKWKKH FHVVA VNRRLRKFP T C P

SEQ ID NO: 180\_AA460132\_H  
 MAAARATTPADGEEPAPAEALAAARERSSRFLSGLELVKQGAEARVFRGRFQGRAAVIK  
 HRFPKGYRHPALEARLGRRRTVQEARALLRCRRAGISAPVVFVDYASNCLYMEEIEGSV  
 TVRDYIQSTMETEKTPQGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLEQLNIV  
 LIDFGLSFISALPEDKGVLDLYVLEKAFLSTHPNTETVFEAFLKSYSTSSKKARPVLKKLD  
 EVRLRGRKRSMVG

SEQ ID NO: 181\_SGK034\_H  
 QREKVNQGNMPGLQSTFLAMDTEEGVEVVWNLHFGDRKAFAAHEEKIQTVFEQLVLVDH  
 PNIVKLHKYWLDTSEACARVIFITEYVSSGSLKQFLKTKKNHKAMNARAWKRWCTQILS  
 ALSFLHACSPPIIHGNLTSDTIFIQHNGLIKIGSVWHRIFSNALPDDLRSPIRAEREELR  
 NLHFFPPEYGEVADGTAVDIFSFGMCALEMAVLEIQTNGDTRVTEEAIAARARHSLSDPNM  
 REFILCCLARDPARRPSAHSLLFHRVLFVHSLKLLAAHCFIQHQYLMPENNVVEEKTAM  
 DLHAVLAELPRPRPPLQWRYSEVSFMELDKFLEDVRNGIYPLMNFAATRPLGLPRVLAP  
 PPEEVQAKTPTPEPFDSETRKVIQMOCNLERSEDKARWHLTLLLVLEDRLHRQLTYDLL  
 PTDSAQDLASELVHYGFLHEDDRMKLA AFLESTFLKYRG TQA

SEQ ID NO: 182\_AA103218\_M SGK034\_M  
 HASAPEYGEVNDGTGFVDIFSFGMCALEMAVLEIQANGDTRVTEEAIAARARHSLSDPNMR  
 EFILSCLARDPARRPSAHNLLFHRVLFVHSLKLLAAHCFIQHQYLMPENNVVEEKTAMD  
 LHAVLAEMPQPHGPPMQWRYSEVSFLELDKFLEDVRNGIYPLMNFAAARPLGLPRVLAPP  
 PEEAQKAKTPTPEPFDSETRKVVQMOCNLERSEDKARWHLTLLLVLEDRLHRQLTYDLLP  
 TDSAQDLAAELVHYGFLHEDDRTKLA AFLETTFLKYRG TQA

SEQ ID NO: 183\_NEK7\_H, N34132\_H  
 MSGGAAEKQSSTPGSLFLSPPAPAPKNGSSSDSSVGEKLGAAAADAVTGRTEEYRRRRHT  
 MDKDSRGAAATTTTTEHRFFRRSVICDSNATALELPGLPLSLPQPSIPAAVPQSAPPEPH  
 REETVTATATSQVAQQPPAAAAPGEQAVAGPAPSTVPSSTSKDRPVSQPSLVGSKEEPP  
 ARSGSGGGSKEPQEERSQQODDIEELETKAVGMSNDGRFLKFDIEIGRGSFKTVYKGLD  
 TETTVEVAWCELQDRKLTKSERQRFKEEAEMLKGLQHPNIVRFYDSWESTVKGKKCIVLV  
 TELMTSGTLKTYLKRFKVMKIKVLRSWCRQILKGLQFLHTRTPLIHRDLKCDNIFITGP  
 TGSVKIGDLGLATLKRASFASVIGTPEFMAPEMYEEKYDESVDVYAFGMCMLEMATSEY  
 PYSECQNAAQIYRRVTSGVKPASFDKVAIPEVKEIEGCIQONKDERYSIKDLLNHAFQ  
 EETGVRVELAEEDDGEKIAIKLWLRIEDIKKLKGKYKDNEAIEFCFDLERDVPEDVAQEM  
 VESGYVCEGDHKTMAKAIKDRVSLIKRKREQRQLVREEQENKKQEESLQKQVEQSSASQ  
 TGIKQLPSASTGIPTASTTSASVSTQVEPEEPEADQHQQLOYYQQPSISVLSDGTVDSGQG  
 SSVFTESRVSSQQTVSYGFPXHEQAHSTGTVPGHIPTSTVQAQSQPHGVYPPSSVQQGIQQ  
 TAPPQQTVQYSLSQSTTSSEATTAQPVSPQAPQVLPQVSAGKQSTQGVVSQVAPAEVAV  
 AQPQATQPTTLASSVDSAHSDVASGMSDGNENVPSSSGRHEGRTTKRHYRKSVRSRSRHE  
 KTSRPKLRI LNVS NKGDRVVECQLETHNRKMVTFKFDLDGDNPEEIATIMVNDFILAIE  
 RESFVDQVREIEKADEMLSEDVSVEPEGDQGLSLOGKDDYGFSGSQKLEGEFKQPIPA  
 SSMPQQIGIPTSSLTQVVHSAGRRFIVSPVPESRLRESKVFPSEITDTVAASTAQSPGMN  
 LSHSASSLSLQAFSELRRQMTEGPNTAPPNFSHTGPTFPVPPFLSSIAGVPTTAAAT  
 APVPATSSPPNDISTSVIQSEVTVPTEEGIAGVATSTGVVTSGGLPIPPVSES PVLSSVV  
 SSITIPAVVSISTTSPSLQVPTSTSEIVVSSTALYPSVTVSATSASAGGSTATPGPKPPA  
 VVSQQAAGSTTVGATLTSVSTTTSFPTASQLSIQLSSSTSTPTLAETVVVSAHSLDKTS

## FIGURE 1P

HSSTTGLAFSLSAPSSSSSPGAGVSSYISQPGGLHPLVIPSVIASTPILPQAAGPTSTPL  
 LPQVPSIPPLVQPVANVPAVQQTLIHSQPPALLPNQPHTHCPEVDSDTQPKAPGIDDIK  
 TLEEKLRSLFSEHSSSGAQHASVSLETSLVIESTVTPGIPTTAVAPSKLLTSTTSTCLPP  
 TNLPLGTVALPVTVPVTPGQVSTPVSTTTSGVKPGTAPSKPPLTKAPVLPVGTLPAGTL  
 PSEQLPFPFGPSLTQSQQPLEDLDAQLRRTLSPEMITVTSAGVPVSMAAPTAITEAGTQP  
 QKGVSVQKEGPVLATSSGAGVFKMGRFQVSVAADGAQKEGKNKSEDAKSVHFESSTSESS  
 VLSSSSPESTLVKPEPNGITIPGISSDVPESAHKTTASEAKSDTGQPTKVGRFQVTTAN  
 KVGRFSVSKTEDKITDTKKEGPVASPPFMDLEQAVLPAVIPKKEKPELSEPSHLNGPSSD  
 PEAAFLSRDVGSGSPHSPHQLSSKSLPSQNLSQLSNSFNSSSYMSSDNESDIEDLDL  
 LELRRLRDKHLKEIQDLQSRQKHEIESLYTKLGKVP PAVIIPPAAPLSGRRRRPTKSKGS  
 KSSRSSSLGNKSPQLSGNLGQSAASVLHPQQT LHPPGNI PESGQNQLLQPLKPSPSDN  
 LYSFTSDGAISVPSLSAPGQGNKATIIVQKQ

SEQ ID NO: 184\_BCON3\_H

MSEGESQTVLSSGSDPKVESSSSAPGLTSVSPVPTSTTSAASPEEEEESEDESEILEESP  
 CGRWQKRREEVNQRNVPIDISAYLAMDTTEGVEVWNEVQFSEKKNYKLQEEKVRAVFDN  
 LIQLEHLNIVKFHKYWADIKENKARVIFITEYMSSGSLKQFLKKTCKNHKTMNEKAWKRW  
 CTQILSALSYLHSCDPPIIHGNLTCDTIFIQHNGLIKIGSVAPDTINNHVKTCTREEQKNL  
 HFFAPEYGEVTNVTTAVDIYSFGMCALEMAVLEIQNGGESSYVPQEAISSAIQLEDPLQ  
 REFIOKCLQSEPARRPTARELLFHPALFEVPSLKLLAAHCIVGHQHMIPENALEEITKNM  
 DTSAVLAEIPAGPGREPVTLYSQSPALEDKFLDVRNGIYPLTAFGLPRPQQPQQEEV  
 TSPVPPSVKTPTEPAEVEVTRKVVLMQCNIESVEEGVKHHLTLLLKLEDKLNRLHSCDL  
 MPNENIPELAAELVQLGFISEADQSRLTSLLEETLNKFNFARNSTLNSAAVTVSS

SEQ ID NO: 185\_AA711829\_M

LKQFLKKTCKNHKTMNEKAWKRWCTQILSALSYLHSCDPPIIHGNLTCDTIFIQHNGLIK  
 IGSVAPDTINNHVKTCTREEQKNLHFFAPEYGEVTNVTTAVDIYSFGMCALEMAVLEIQN  
 GESSYVPQEAISSAIQLEDLSLQREFIOKCLQSEPARRPTARELLFHPALFEVPSLKLLA  
 AHCIVGHQHMIPENALEEITKNMDTSAVLAEIPAGPGREPVTLYSQSPALEDKFLDVR  
 RYNGIYPLTAFGLPRPQQPQQEEVTSPVPPSVKTPTEPAEVEVTRKVVLMQCNIESVEEG  
 VKHHLTLLLKLEDKLNRLHSCDLMPNESIPDLAAELVQLGFISEADQSRLTSLLEETLNK  
 FNFTRNSTLNTATVTVSS

SEQ ID NO: 186\_AA099102\_H

MSSCVSSQPSSNRAAPQDELGGRGSSSESQKPCEALRGLSSLSIHLGMESFIVVTECEP  
 GCAVDLGLARDRPLEADGQEVPLDTSGSQARPHLSGRKLSLQERSQGGLAAGSLDMNGR  
 CICPSLPYSPVSSPQSSPRLPRRPTVESHHVSITGMQDCVQLNQYTLKDEIGKGSYGVMK  
 LAYNENDNTYYAMKVLSKKKLIRQAAFPRRPPPRGTRPAPGGCIQPRGPIEQVYQEIAIL  
 KKLDPNVVVLVEVLDDPNEDHLYMVFEVLNQGPVMEVPTLKPLSEDQARFYFDLIKGI  
 EYLHYQKIIHRDIKPSNLLVGEDGHIKIADFGVSNEFKGSDALLSNYVGTPAFMAPESLS  
 ETRKIFSGKAKDVWAMGVTLVCFVFGQCPFMDERIMCLHSKIKSQALEFPDQPDIAEDLK  
 DLI TRMLDKNPESRIVVPEIKLHPVWTRHGAELPSEDENCTLVEVTEEEVENSVKHIPS  
 LATVILVKTMIRKRSFGNPFEGSRREERSLSAPGNLLTKKPTRECESLSELKEARQRRQP  
 PGRHPAPRGGGSALVRGSPCVESCWAPAPGSPARMHPLRPEEAMEPE

SEQ ID NO: 187\_5R69\_17\_2\_H

MQEIPQEQIKEIKKEQLSGSPWILLRENEVSTLYKGEYHRAPVAIKVFKKLQAGSIAIVR  
 QTFNKEIKTMKKFESPNILRIFGICIDETVTPPQFSIVMEYCELGTRELLDREKDLTLG

## FIGURE 1Q

KRMVLVLGAARGLYRLHHSEAPELHGKIRSSNFLVTQGYQVKLAGFELRKTQTSM SLGTT  
 REKTD RVKSTAYLSPQELEDV FYQYDV KSEIYSFGIVLWEIATGDI PFQGE ECEDWLSQW  
 L

SEQ ID NO: 188\_H85811\_H  
 MAPVYEGMASHVQVFS PHTLQSSAFCSVKKLKIEPSSNWD MTGYGSHSKVYSQSKNIP LS  
 QPATTTVSTSLPVPNPSPYEQ TIVFP GSTGHI VVTSASSTSVTGQVLGGPHNLMRRSTV  
 SLLDTYQKCGLKRKSEEI ENTSSVQIIEEHPPMIQNNASGATVATATTSTATSKNSGNS  
 EGDYQLVQHEVLCSMTNTYEVLEFLGRGT FGQVVKCWKRG TNEIVAIKILKNHPSYARQG  
 QIEVSILARLSTESADDYNFVRAYECFQHKHNTCLVFEMLEQNLYDFLKQNKFSPLPLKY  
 IRPVLQQVATALMKLSLGLIHADLKPENIMLVDP SRQPYRVKVIDFGSASHVSKAVCST  
 YLQSRYYRAPEIILGLPFCEAIDMWSLGCVIAELFLGWPLYPGDSEYDQIRYISQTQGLP  
 AEYLLSAGTKTTRFFNRD TDSPLYPLWRLKTPDDHEAETGIKSKEARKYIFNCLDDMAQVN  
 MTTDLEGS DMLVEKADRREFIDLLKKMLTIDADKRITPIETLNHPFVTMT HLLDFPHSTH  
 VKSCFQNM EICKRRVNMYDTVNQSKTPFITHVAPSTSTNLTMTFNNQLTTVHNQPSAASM  
 AAVAQRSMPLQTGTAQICARPD PFQQA LIVCP PGFQGLQASPSKHAGYSVRMENAVPIVT  
 QAPGAQPLQIQPGLLAQQAWPSGTQQI LLPPAWQQLTG VATHTSVQHATVIPETMAGTQQ  
 LADWRNTHAHGSHYNPIMQQPALLTG HVTLPAAQPLNVGV AHVMRQQPTSTTSSRKSKQH  
 QSSVRNVSTCEVSSSQAISSPQRSKR VKENTPPRCAMVHSSPACSTSVTCGWGDVASSTT  
 RERQRQTIVIPDTPSPTVSVITISSDTDEEEEQKHAPTSTVSKQRKNVISCVTVHDS PYS  
 DSSSNTSPYSVQQRAGHNNANAFDTKGSLE NHCTGNPRTIIVPPLKTQASEVLVECD SLV  
 PVNTSHHSSSYKSKSSSNVTSTSGHSSGSSSGAITYRQQRPGPHFQQQQPLNLSQAQQHI  
 TTDRTGSHRRQAYITPTMAQAPYSFPHNSPSHGT VHPHLAAAAAAHLPTQPHLYTYTA  
 PAALGSTGTVAHLVASQGSARHTVQHTAYPASIVHQPVPVSMGPRVLPSP TIHPSQYPAQF  
 AHQTYISASPASTVYTYGYPLSPAKVNQYPYI

SEQ ID NO: 189\_DYRK3\_H  
 MMIDETKCPPCSNVL CNPSEPPPPRRRLNMTAEQFTGDHTQHFLDGGEMKVEQLFQEFGNR  
 KSNTIQSDGISDSEKCSPTVSQ GKSSDCLNTVKSNSSSSKAPKV VPLTPEQALKQYKHHLT  
 AYEKLEIINYPEIYFVGPN AKKRHGVIGGPNNGGYDDADGAYIHVPRDHLAYRYEVLKII  
 GKGSFGQVARVYDHLRQYVALKMVRNEKRFHRQAABEIRILEHLKKQDKTGS MNVIHML  
 ESFTFRNHVCMAFELLSIDLYELIKKNKFQGF SVQLVRKFAQSILQSLDALHKNKI IHCD  
 LKPENILLKHHGRSSTKVIDFGSSCFEYQKLYTYIQSRFYRAPEIILGSRYSTPIDIWSF  
 RCILAE LLTGQPLFPGEDEGDQLACMMELLGMPPPKLLEQSKRAKYFINSKGI PRYCSVT  
 TQADGRVVLVGGRSRRGKKRGPPGSKDWGTALKGCD DYLFI EFLKRCLHWDPSARLTPAQ  
 ALRHPWISKSVPRPLTTIDKVS GKR VNPASAFQGLGSKLPPVVG IANKLKANLMSETNG  
 SIPLCSVLPKLIS

SEQ ID NO: 190\_AA589241\_M DYRK3\_M  
 TRPELLGMPPQKLLEQSKRAKYFINSKGLPRYCSVSTQTDGRVVL LGGRSRRGKKRGPPG  
 SKDWATALKGCGDYLFIEFLKRCLQWDPSARLTPAQALRHPWISKSTPKPLTMDKVP GKR  
 VVNPTNAFQGLGSKLPPVVG IASKLKANLMSETSGSIPLCSVLPKLIS

SEQ ID NO: 191\_5R72\_16\_2\_H  
 MAGGRGAPGRGRDEPPESYPQRQDHELQALEAIYGADFQDLRPDACGPVKEPPEINLVLY  
 PQGLTGEEVYVKVDLRVKCPPTYPDVVPEIELKNAKGLSNESVNLLKSRLEELAKKHCGE  
 VMIFELAYHVQSFLSEHNKPPPKSFHEEMLERRAQEEQQRLLEAKRKEEQEQREILHEIQ  
 RRKEEIKKEKKRKEMAKQERLEIASLSNQDHTSKKDPGGHRTAAILHGGS P D FVGN GKHR  
 ANSSGRSRRERQYSVCNSEDSPGSCEILYFNMGSPDQLMVHKGKCI GSDEQLGKL VYNAL  
 ETATGGFVLLYEWVLQWQKMGPF LT SQEKEKIDKCKKQIQGTETEFNSLVKL SHPNVVR



## FIGURE 1R

YLAMNLKEQDDSI VVDILVEHISGVSLAAHLSHSGPI PVHQLRRYTAQLLSGLDYLSHSNS  
VVHKVLSASNVLVDAEGTVKITDYSISKRLADICKEDVFEQTRVRFSDNALPYKTGKKGD  
VWRLGLLLLLSLSQGECEYPTI PSDLPADFQDFLKKCVCLDDKERWSPQQLLKHSFIN  
PQPKMPLVEQSPEDSGGQDYVETVI PSNRLPSAAFFSETQRQFSRYFIEFEELQLLGKGA  
FGAVIKVQNKLDGCCYAVKRI PINPASRQFRRIKGEVTLLSRLHHENIVRYNAWIERHE  
RPAGPGTPPPDSGPLAKDDRAARGQPASDTDGLDSVEAAAPPPILSSSVIEWSTSGERSAS  
ARFPATGPGSSDDEDDDEDEHGGVFSQSFLPASDSEDI IFDNEDENSKSNQDEDCNEK  
NGCHESEPSVTTEAVHYLYIQMEYCEKSTLRDTIDQGLYRDTVRLWRLFREILDGLAYIH  
EKGMHRDLKPVNIFLDSDDHVKIGDFGLATDHLAFSADSKQDDQTDGLIKSDPSGHLTG  
MVGTAlyVSPVQGSTKSAYNQKVDLFSLGIIFFEMSYHPMVTASERIFVLNQLRDPTSP  
KFPEDFDDGEHAKQKSVISWLLNHDPAKRPTATELLKSELLPPPQMEESSELHEVLHHTLT  
NVDGKAYRTMMAQIFSQRISPAIDYTYDSDILKGNFSIRTAKMQQHVCTIIRIFKRHGA  
VQLCTPLLLPRNRQIYEHNEAALFMDHSGMLVMLPFDLRIPFARYVARNNILNLKRYCIE  
RVFRPRKLDRFHPKELLECAFDIVTSTTNSFLPTAEIITYTIEIIQEFPALQERNYSIYL  
NHTMLLKAILLHCGIPEDKLSQVYIILYDAVTEKLTRREVEAKFCNLSLSSNSLCRLYKF  
IEQKGLDQDLMPTINSLIKQKTGIAQLVKYGLKDLEEVVGLLKKLGKIKLQVLINLGLVYK  
VQQHNGIIFQFVAFIKRRQRAVPEILAAAGGRYDILLIPQFRGPQALGPVPTAIGVSIADK  
ISAAVLNMEESVTISSCDLLVSVSGQMSMSRAINLTQKLWTAGITAEIMYDWSQSQEELQ  
EYCRHHEITYVALVSDKEGSHVKVKSFEKERQTEKRVLETELVDHVLQKLRTKVTDERNQ  
REASDNLAVQNLKGSFSNASGLFEIHGATVVPIVSVLAPEKLSASTRRRYETQVQTRLQT  
SLANLHQKSSEIEILAVDLPKETILQFLSLEWDADEQAFNTTVKQLLSRLPKQRYLKLVC  
DEIYNIKVEKKVSVLFLYSYRDDYRILF

SEQ ID NO: 192\_R43524\_H, HRI\_H  
MLGGNSGVRKREEEGDAGAVAAPPAIDFPAEGPDPEYDESDVPAEQVLKEPLQQPTFP  
FAVANQLLLVSLLEHLSHVHEPNPLRSRQVFKLLCQTFIKMGLLSSFTCSDEFSSLRLHH  
NRAITHLMRSAKERVRQDPCEDISRIQKIRSREVALEAQTSRYLNEFEELVILGKGGYGR  
VYKVRNKLDGQYYAIKKILIKGATKTVCMKVLREVKVLAGLQHPNIVGYHTAWIEHVHVI  
QPRADRAAIELPSLEVLSDQEEDEQCGVKNDSSSSSIIFAEPTPEKEKRFGESDTENQ  
NNKSVKYTTNLVIRESGELESTLELQENGLAGLSASSIVEQQPLRRNSHLEESFTSTEE  
SSEENVNFLGQTEAQYHMLHIQMQLCELSLWDWIVERNKRGREYVDESACPYVMANVAT  
KIFQELVEGVFYIHNMGIVHRDLKPRNIFLHGPDQQVKIGDFGLACTDILQKNTDWTNRN  
GKRTPTHTSRVGTCLYASPEQLEGSEYDAKSDMYSLGVVLELFPFGTEMERA EVLTGL  
RTGQLPESLRKRCVPQAKYIQHLTRRNSSQRPSAIQQLQSELFQNSGNVNLTLMKII EQ  
EKEIAELKKQLNLLSQDKGVRDDGKDGGVG

SEQ ID NO: 193\_17000057519457\_H  
MAAARATTPADGEEPAPAEALAAARERSRFLSGLELVKQGAEARVFRGRFQGRAAVIK  
HRFPKGYRHPALEARLGRRRTVQEARALLRCRRAGISAPVVFFVDYASNCLYMEEIEGSV  
TVRDYIQSTMETEKTPQGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLEQLNIV  
LIDFGLSFISALPEDKGVLDLYVLEKAFLSTHPNTETVFEAFLKSYSTSSKKARPVLKKLD  
EVRLRGRKRSMVG

SEQ ID NO: 194\_AA013524\_M  
LVQQGAEARVFRGRFQGRAAVVKHRFPKSYRHPELEARLGRRRTVQEARALLRCRRAGIA  
APVVFFVDYASNCLYMEEIEDSVTVRDYIQSTMETEKDPQCLLDLARRMGQVLAMHDQD  
LIHGDLTTSNMLLRRPLAQLHIVLIDFGLSFVSGLPEDKGVLDLYVLEKAFLSTHPHTETA  
FEAFLKSYGASSKKSSPVLKKLDEVRLRGRKRSMVG



## FIGURE 1S

SEQ ID NO: 195\_17000139801197\_H, IRAKM\_H  
MAGNCGARGALSAHTLLFDLPPALLGELCAVLDS CDGALGWRGLAERLSSSWLDVRHIEK  
YVDQGKSGTRELLWSWAQKNKTIGDLLQVLQEMGHRRRAIHLITNYGAVLSPSEKSYQEGG  
FPNILFKETANVTVDNVLIP EHNKGVLLKSSISFQNIIEGTRNFHKDFLIGEGEIFEVY  
RVEIQNLTYAVKLFKQEKMKQCKKHWRFLSELEVLLL FHHPNILELAAYFTETEFCL  
YPYMRNGTLFDRLQCVGDTAPLPWHIRIGILIGISKAIHYLHNVPQCSVICGSISSANIL  
LDDQFQPKLTDFAMAHFRSHLEHQ SCTINMTSSSSKHLWYMPEEYIRQGKLSIKTDVYSF  
GIVIMEVLTGCRVVLDDPKHIQLRDLRELMEKRGLD SCLSFLDKKVP PCPRNFS AKLFC  
LAGRCAATRAKLRPSMDEV LNTLESTQASLYFAEDPPTSLKSFRCPSPLFLENVPSIPVE  
DDESQNNNLLPSDEGLRIDRMTQKTPFECSQSEVMFLSLDKKPESKRNEEACNMPSSSCE  
ESWFPKYIVPSQDLRPYKVNIDPSSEAPGHSCSRPVESSCSSKFSWDEYEYQYKKE

SEQ ID NO: 196\_AA840598\_M IRAKM\_M  
MWKRFLSELEVLLLFRHPHILELAAYFTETEKLC LVYPYMSNGTLFDRLQCTNGTTPLSW  
HVRISVLIGIAKAIQYLHNTQPCAVICGNVSSANILLDDQLQPKLTDFAAAHFRPNLEQQ  
SSTINMTGGGRKHLWYMPEEYIRQGRLSVKTDVYSFGIVIMEVLTGCKVVLDDPKHVQLR  
DLLMELMEKRGLD SCLSFLDRKI PP CPRNFS AKLFLAGRCVATKAKLRPTMDEVLSLE  
STQPSLYFAEDPPTSLKSFRCPSPLFLDNVPSIPVEDDENQNNH SVPPKEVLGTDRTVQK  
TPFECSQSEVTFGLDRNRGNRGSEADCNPVSSSHEECWSPELVAPSQDLSPTVISLGSS  
WEVPGHSYGSKPMEKRCSSGLFCSEHEQSKKQ

SEQ ID NO: 197\_AA088547\_H  
MASAVRGSRPWPRLGLQLQFAALLGLTSPQVHTLRPENLLL VSTLDGSLHALSKQTGDL  
KWTLRDDPVI EGPMYVTEMAFLSDPADGSLYILGTQKQQLMKLPFTIPELVHASPCRSS  
DGVFYTGKQDAWFVVD PESGETQMTLTTEGPSTPRLYIGRTQYTVTMHDPRAPALRWNT  
TYRRYSAPPMDGSPGKYMSHLASCGMGLLLTVDPGSGTVLWTQDLGVPVMGVYTWHDGL  
RQLPHLT LARDTLHFLALRWGHIRLPASGPRDTATL FSTLDTQLLMTLYVGKDETGFYVS  
KALVHTGVALVPRGLTLAPADGPTTDEVTLQVSGEREGSPSTAVRYP SGVALPSQWLLI  
GHHELPPVLHTTMLRVHPTLGSGTAETRPPENTQAPAFFLELLSLSREKLWDSELHPEEK  
TPDSYLGLGPQDLLAASLTAVLLGGWILFVMRQVVEKQOETPLAPADFAHISQDAQSLHS  
GASRRSQKRLQSPSKQAQPLDDPEAEQLTVVGKISFNPKDVLGRGAGGTFVFRGQFEGRA  
VAVKRLRECFLVRREVQLLQESDRHPNVLRYFCTERGPOFHYIALELCRASLQEYVEN  
PDLDRGGLEPEVVLQQLMSGLAHLHSLHI VHRDLKPGNILITGPD SQGLGRVVLSDFGLC  
KKLPAGRCFSLSHSGIPGTEGWMAPELLQLLPDSPTS AVDI FSAGCVFYVLSGGSHPF  
GDSLYRQANILTGAPCLAHLEEVHDKVVARDLVGAMLSPLPQPRPSAPQVLAHPFFWSR  
AKQLQFFQDVSDWLEKESEQEPLVRALEAGGCAVVRDNWHEHIS MPLQTDLRKFRSYKGT  
SVRDLLRAVRNKKHHYREL PVEVRQALGOVPDGFVQYFTNRFPRLLLHTHRMRSCASES  
LFLPYPPDSEARRPCPGATGR

SEQ ID NO: 198\_HGP\_6644466  
MEGISNFKTPSKLSEKKKSVLCSTPTINIPASPFMQKLGF GTGVNVYLMKRSRGLSHSP  
WAVKKINPICNDHYRSVYQKRLMDEAKILKSLHHPNIVGYRAFTEANDGSLCLAMEYGGG  
KSLNDLIEERYKASQDPFPAIILKVALNMARGLYLHQEKLLHGD IKSSNVVIKGD FE  
TIKICDVGVSPLDENMTVTDPEACYIGTEPWKPKEAVEENGVI TDKADIFAFGLTLWEM  
MTLSIPHINLSNDDDDDKTFDESDFDDEAYYAALGTRPPINMEELDESYQKVIELFSVC  
TNEDPKDRPSAAHIVEALET DV

SEQ ID NO: 199\_AA449542\_M  
SPRGLSHSPWAVKKISLLCDDHYRTVYQKRLTDEAKILKNLNHPNIGYRAFTEASDGSL  
CLAMEYGGEKSLNDLIEERNKDSGSPFPAAVILRVALHMARGLYLHQEKLLHGD IKSS

## FIGURE 1T

NVVIKGFETIKICDVGVSPLDENMTVTDPEACYIGTEPWKPKEALEENGIITDKADV  
AFGLTLWEMMTLCIPHVNLPDDDDVEDATFDESDFDDEAYYAALGTRPSINMELDDSYQK  
AIELFCVCTNEDPKDRPSAAHIVEALELDGQCCGLSESKH

SEQ ID NO: 200\_5R57\_10\_2\_M TESK2\_M  
LLDSDLYLPTVRVKLAYGIAVGLSYLHFKGIFHRDLTSKV

SEQ ID NO: 201\_AA232253\_H  
MSSLGASFVQIKFDDLQFFENC GGGSFGSVYRAKWISQDKEVAVKLLKIEKEAEILSVL  
SHRNIIQFYGVILEPPNYGIVTEYASLGSLYDYINSNRSEEMDMDHIMTWATDVAKGMHY  
LHMEAPVKVIHRDLKSRNVVIAADGVLKICDFGASRFHNHTTHMSLVGTFPWMAPEVIQS  
LPVSETCDTYSYGVVLWEMLTREVPFKGLEGLQVAWLVEKNERLTIPSSCPRSFAELLH  
QCWEADAKKRPSFKQIIISILESMSNDTSLPDKCNSFLHNKAWEWRCEIEATLERLKKLERD  
LSFKEQELKERERRLKMWEQKLTEQSNTPLLPSFEIGAWTEDDVYCWVQQLVRKGDSSAE  
MSVYASLKFENNITGKRLLLLLEEDLKDMGIVSKGHIHFKSAIEKLTHDYINLFHFPPL  
IKDSGGPEEENEKIVNLELVFGFHLKPGTGPQDCKWKMYMEMDGDEIAITYIKDVTFTNT  
NLPDAEILKMTKPPFVMEKWIVGIAKSQTVECTVITYESDVRTPKSTKHVHLIQWSRTKPQ  
DEVKAVQLAIQTLFTNSDGNPGSRSDSSADCQWLDTLRMRQIASNTSLQRSQSNPILGSP  
FFSHFDGQDSYAAAVRRPQVPIKYQQITPVNQSRSSSPTQYGLTKNFSSLHLNSRDSGFS  
SGNTDTSSERGRYSDRSRNKYGRGSI SLNSSPRGRYSGKSQHSTPSRGRYPGKFYRVSQS  
ALNPHQSPDFKRSRDLHQPNITPGMPLHPETDSRASEEDSKVSEGGWTKVEYRKKPHRP  
SPAKTNKERARGDHRGWRNF

SEQ ID NO: 202\_AI375137\_H  
MGNYKSRTQTCTDEWKKKVSESYVITIERLEDDLQIKEKELTELNRNIFGSDEAFSKVNL  
NYRTENGLSLLHLCCICGGKKSHIRTLMLKGLRPSRLTRNGFTALHLAVYKDNAELITSL  
LHSGADIQQVGYGGLTALHIATAGHLEAADVLLQHGANVNIQDAVFFTPLHIAAAYYGHE  
QVTRLLLKFGADVNVSGEVGDRPLHLASAKGFLNIAKLLMEEGSKADVNAQDNEDHVPLH  
FCSRFGHHDIVKYLLOSDLEVQPHVNNIYGDTPHLHLACYNGKFEVAKETIIQISGTESLTK  
ENIFSETAFHSACTYGKSIDLKFLLDQNVININHQGRDGTGLHSACYHGHIRLVQFLL  
DNGADMNLVACDPSRSSGEKDEQTCMLWAYEKGHDAIVTLLKHYKRPQDELPCNEYSQPG  
GDGSYVSVSPPLGKIKSMTKEKADILLRAGLPSHFHLQLSEIEFHEIIGSGSFGKVYKG  
RCRNKIVAIKRYRANTYCSKSDVDMFCREVSILCQLNHPCVIOFVGACLNDRPSQFAIVTQ  
YISGGSLSFLLHEQKRILDLQSKLIIAVDVAKGMEYLHNLTQPIIHRDLNSHNILLYEDG  
HAVVADFGESRFLQSLDEDNMTKQPGNLRWMAPEVFTQCTRYTIKADVFSYALCLWEILT  
GEIPFAHLKPAADMAHYYHIRPPIGYSIPKPISSLLIRGWNACPEGRPEFSEVVMKLE  
ECLCNIELMSPASSNSSGSLSPSSSSDCLVNRGGPGRSHVAALRSRFELEYALNARSYAA  
LSQSAGQYSSQGLSLEEMKRSLOQYTPIDKYGYVSDPMSSMHFHSRNSSSSFEDSS

SEQ ID NO: 203\_H97685\_H  
MESERSPLYRQLIDLGYLSSSHWNCGAPGQDTKAQSMLEQSEKLRHLSTFSHQVLQTRL  
VDAAKALNLVHCHCLDIFINQAFDMQRDLQITPKRLEYTRKKENELYESLMNIANRKQEE  
MKDMIVETLNTMKEELLDDATNMEFKDVIVPENGEVGTREIKCCIRQIQELIISRLNQA  
VANKLISSVDYLRFSVGTLERCLOSLEKSQDVSVHITSNYLKQILNAAHYHEVTFHSGS  
SVTRMLWEQIKQIIQRITWVSPPAITLEWKRKVAQEAIESLSASKLAKSICSQFRTRLNS  
SHEAFAASLRQLEAGHSGRLEKTEDLWLRVRKDHAPRLARLSLESRLQDVLLHRKPKLG  
QELGRGQYGVVYLCDNWGGHFPALKSVVPPDEKHWNDLALEFHMYRSLPKHERLVDLHG  
SVIDYNYGGGSSIAVLLIMERLHRDLTYTGLKAGLTLETRLQIALDVVEGIRFLHSQGLVH  
RDIKLNVLDDKQNRAKITDLGFCKPEAMMSGSI VGTPIHMAPELFTGKYDNSVDVYAFG

## FIGURE 1U

ILFWYICSGSVKLPEAFERCASKDHLWNNVRRGARPERLPVFDEECWQLMEACWDGDPLK  
RPLLGI VQ PMLQ GIMNRLCKSNSEQPNRGLDDST

SEQ ID NO: 204\_W20810\_M  
DVNLKASKASDVYSFGILVWAVLAGREAELVDKTSLIRETVCDRQSRPPLTELPPGSPET  
PGLEKLKELMIHCWGSQSENRP SFQDCEPKTNEVYNLVKDKVDAAVSEVKHYLSQHRSSG  
RNLSAREPSQRGTEMDCPRETMVSKMLDRLHLEEPSGVPVPGKCPERQAQDTSVGPATPAR  
TSSDPVAGTPQIPHTLPFRGTTGPGVFTETPGPHQQRNQGDGRHGTPWYPWTPPNPMTGP  
PALVFNNCSEVQIGNYNLSLVAPPRTTASSSAKYDQAQFGRGRGWQPFHK

SEQ ID NO: 205\_AA744236\_H  
MGSENSALKSYTLREPPFTLPSGLAVYPAVLQDGKFASVFVYKRENEDKVNKAACHLCTL  
RHPCLLRFLSCTVEADGIHLVTERVQPLEVALETLSAEVCAGIYDILLALIFLHDRGHL  
THNNVCLSSVFVSEDGHWKLGGMETVCKVSQATPEFLRSIQSIRD PASI PPEEMSPEFTT  
LPECHGHARDAFSFGTLVESLLTILNEQVSADVLSSFQOTLHSTLLNPIPKCRPALCTLL  
SHDFFRNDLFLEVNF LKSLTLKSEEEKTEFFKFLDRVSLSEELIASRLVPLLLNQLVF  
AEPVAVKSFLPYLLGPKKDHAQGETPCLLSPALFQSRVIPVLLQLFEVHEEHVRMVLLSH  
IEAYVEHFTQEQLKKVILPQVLLGLRDTSDSIVAITLHSLAVLVSLLGPEVVGGERTKI  
FKRTAPSFTKNTDLSLEGDPFSQPIKFPINGLSDVKN TSEDS ENFPSSSKKSEEPDWSE  
PEEPENQTVNIQIWPREPCDDVKSQCTTLDVEESSWDDCEPSSLDTKVNPGGGITATKPV  
TSGEQKPIPALLSLTEESMPWKSSLPQKISLVQRGDDADQIEPPKVSSQERPLKVPSELG  
LGEEFTIQVKKKPVKDPMDWFADMIPEIKPSAAFLILPELRTEMVPKKDDVSPVMQFSS  
KFAAAEITEGEAEGWEEEGELNWNEDNNW

SEQ ID NO: 206\_AI052250\_H  
MESMLNKLKSTVTKV TADVTSAVMGIPVTREFDVGRHIASGCNGLAWKIFNGTKKSTKQE  
VAVFVFDKKLIDKYQKFEKDQIIDSLKRGVQQLTRLRHPRLLT VQHPLEESRDCLAFCTE  
PVFASLANVLGNWENLPSPISPDIKDYKLYDVETKYGLLQVSEGLSFLHSSVKMVHGNIT  
PENIILNKSGAWKIMGFD FCVSSTNPSEQEPKFPCKEWDPNLPSLCLPNPEYLAPEYILS  
VSCETASDMYSLGTVMYAVFNKGKPIFEVNKQDIYKSFSRQLDQLSRLGSSSLTNIPEEV  
REHVKLLLNVTPTVRPDADQMTKI PFFDDVGAVTLQYFDTLFQRDNLQKSQFFKGLPKVL  
PKLPKRVI VQRILPCLTSEFVNPDMPFVLPNVLLIAEECTKEEYVKLILPELGPVFKQQ  
EPIQILLIFLQKMDLLT KTPPDEIKNSVLPVMYRALEAPSIQIQELCLNI IPTFANLID  
YPSMKNALIPRIKNACYKHLPLRFV

SEQ ID NO: 207\_AA278842\_H  
MWFFARDPVRDPPFELIPEPPEGGLPGPWALHRGRKKATGSPVSI FVYDVKPGAEEQTQV  
AKAAFKRFKTLRHPN ILAYIDGLETEKCLHVVT EAVTPLGIYLKARVEAGGLKELEISWG  
LHQIVKALSFLVNDCSLIHNNVCM AAVFVDRAGEWKLGGLDYMYSAQGN GGGPPRKG IPE  
LEQYDPPELADSSGRVVREKWSADMWRLGCLIWEVFNGPLPRAAALRNPGKIPKTLVPHY  
CELVGANPKVRPNPARFLQNCRAPGGFMSNRFVETNLFLEEIQIKEPAEKQKFFQELSKS  
LDAFPEDFCRHKVLPQLLTAF EFGNAGAVLTPLFKVGKFLSAEEYQQKIIPVVVKMFSS  
TDRAMRIRLLQQMEQFIQYLDEPTVNTQIFPHVHGF LDTNPAIREQT VKSMLLLAPKLN  
EANLNVELMKHFARLQAKDEQGPIRCNTTVCLGKIGSYLSASTRHRVLTSAFSRATRDPF  
APSRVAGVLGFAATHNLYSMNDCAQKILPVLGCLTV DPEKSVRDQAFKAIRSFLSKLESV  
SEDPTQLEEEVEKD VHAASSPGMGGAASWAGWAVTGVS SLTSKLIRSHPTTAPTETNIPO  
RPTPEGVPAPAPTVPATPTTSGHWETQEEDKDTAEDSSTADRWDDEDWGSLEQEAESVL  
AQQDDWSTGGQVSRASQVNSDHKSSKSPESDWSSWEAEGSWEQGWQEPSSQEP PPDGTR  
LASEYNWGGPSSDKGDPFATLSARPSTQPRPDSWGEDNWEGLETD SRQVKAELARKKRE  
ERRREMEAKRAERKVAKGPMKLGARKLD

## FIGURE 1V

SEQ ID NO: 208\_AA599286\_H  
 MAFMEKPPAGKVLDDTVPLTAAIEASQSLQSHTEYIIRVQGGISVENSWQIVRRYSDFD  
 LLNNSLQIAGLSLPLPPKKLIGNMDREFIAERQKGLQNYLNVITTNHILSNCELVKKFLD  
 PNNYSANYTEIALQQVSMFFRSEPKWEVVEPLKDIGWRIRKKYFLMKIKNQPKERLVLWS  
 ADLGPDKYLSKDFQCLIKLLPSCLHPYIYRVTFATANESSALLIRMFNEKGTLDLIYK  
 AKPKDPFLKKYCNPKKIQGLELQQIKTYGRQILEVLKFLHDKGFPYGHLLHASNVMLDGD  
 CRLLDLENSLLGLPSFYRSYFSQFRKINTLESVDVHCFGHLLYEMTYGRPPDSVPVDSFP  
 PAPSMVAVVLESTLSCEACKNGMPTISRLLQOMPLFSDVLLTSEKPPQFKIPTKLKEALR  
 IAKECIEKRLIEEQKQIHQHRRLTRAQSHHGSEEERKKRKILARKKSKRSALENSEEHS  
 KYSNSNNSAGSGASSPLTSPSSPTPPSTSGISALPPPPPPPPPPAAPLPPASTEAPAQLS  
 SQAVNGMSRGALLSSIQNFQKGTLRKAKPVI TVLRRSAEASCLHLEGKVLFPYSYSPLPN  
 YPLPGKVIAEPVQPQTVLFCRCSCCKQLFERNNSLSRIKLGWHAKKKKK

SEQ ID NO: 209\_AA425725\_H  
 MSASTGGGGDSGGSGGSSSSSQASCGPESSGSELALATPVPQMLQGLLGSDDEEQEDPKD  
 YCKGGYHPVKIGDVFNGRYHVVRKLGWGHFSTVWLCWDIQRKRFVALKVKSAGHYTETA  
 VDEIKLLKCVRSDSPDPKRETIVQLIDDFRISGVNGVHVCMVLEVLGHQLLKWIIKSNY  
 QGLPVPCKVKSIVRQVLHGLDYLTCKKIHTDIKPENILLCVGDAYIRRLAAEATEWQQA  
 GAPPSPRSIVSTAPQEVLTGKLSKNKRKKMRKRKQKRLLEERLRDLQRLAEMAATQA  
 EDGSLRLDGGSGSTSSSGFSGSLFSPASCISILSGSSNQRETGGLLSPSTPFGASNLLVNP  
 LEPQNAKIKIKIADLGNACWVHKHFTEDIQTRQYRAVEVLIGAEGPPADIWSTACMAF  
 ELATGDYLFEPHSGEDYSRDEDHIAHIVELLGDI PPAFALSGRYSREFFNRRGELRHIHN  
 LKHGGLYEVLMEKYEWPLEQATQFSAFLLPMMEYIPEKRASAADCLQHPWLN

SEQ ID NO: 210\_SGK022\_H  
 MEDFLLSNGYQLGKTIGEGTYSKVKEAFSCKKHQRKVAIKVIDKMGGPSEFIQRFPLPRELQ  
 IVRTL DHKNI IQVYEMLESADGKICLVME LAEGGDVFD CVLN GGPLPESRAKALFRQMVE  
 AIRYCHGCGVAHRDLKCENALLQGFNLKLTDFGFAKVLPKSHRELSQTF CGSTAYAAPEV  
 LQGI PHDSKKGDVWSMGVVLVYMLCASLPFDDTDIPKMLWQQQKGVSFPTHLSI SADCQD  
 LLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 211\_AA060026\_M SGK022\_M  
 MEDFLLSNGYQLGKTIGEGTYSKVKEAFSCKKHQRKVAIKI IDKMGGPEEFIQRFPLPRELQ  
 IVRTL DHKNI IQVYEMLESADGKIYLVME LAEGGDVFD CVLN GGPLPESRAKALFRQMVE  
 AIRYCHGCGVAHRDLKCENALLQGFNLKLTDFGFAKVLPKSRRELSQTF CGSTAYAAPEV  
 LQGI PHDSKKGDVWSMGVVLVYMLCASLPFDDTDIPKMLWQQQKGVSFPTHLGISTECQD  
 LLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 212\_AA399669\_H  
 MGKGDVLEAAPTTTAYHSLMDEYGYEVGKAIGHGSYGSVYEAFTKQKVMVAVKII SKKK  
 ASDDYLNKFLPREIIQQVMKVL RHKYLINFYRAIESTSRVYIILELAQGGDVLEWIQRYGA  
 CSEPLAGKWFSQTLGLIAYLHKSIVHRDLKLENLLLDKWENVKISDFGFAKMVPSNQPV  
 GCSPXYRQVNCFSHLSQTYCGSFAYACPEILRGLPYNPFLSDTWSMGVILYTLVVAHLFP  
 DDTNLKLLRETQKEVTFPANHTISQECKVQLLIACVAQWRKTQARPLSPLL

SEQ ID NO: 213\_AA758539\_H  
 MDDATVLRKKGIVGINLGKGSYAKVKSAYSERLKFNAVAKIIDRRKTPTDFVERFLPRE  
 MDILATVNHGSI IKTYEIFETSDGRIYIIMELGVQGDLLFEIKCQ GALHEDVARKMFRQL  
 SSAVKYCHDLDIVHRDLKCENLLLDKDFNIKLSDFGFSKRCLRDSNGRIILSKTFCGSAA

## FIGURE 1W

YAAPEVLQSIPIYQPKVYDIWSLGVILYIMVCGSMPYDDSDIRKMLRIQKEHRVDFPRSKN  
 LTCECKDLIYRMLQPDVSQLRHIDEILSHSWLQPPKPKATSSASFKEGEGKYRAECKLD  
 TKTGLRPDHRPDHKLGAKTQHRLLVVPENENRMEDRLAETSLAKDHHISGAEVGKAST

SEQ ID NO: 214\_AA883975\_H  
 MSGDKLLSELGYKLGRTIGEGSYSKVKVATSKKYKGTVAIKVVDRRRAPPDFVNKFLPRE  
 LSILRGVRPHIVHVFIEVCNGKLYIVMEAAATDLLQAVQRNGRIPGVQARDLFAQIA  
 GAVRYLHDHHLVHRDLKCENVLLSPDERRVKLTDFGFGRAHGYPDSTTYCGSAAYASP  
 EVLLGIPYDPKKYDVWSMGVLYVMVTGCMFDDSDIAGLPRRQKRGVLYPEGLELSERC  
 KALIAELLQFSPSARPSAGQVARNCWLRAAGDSG

SEQ ID NO: 215\_AA905446\_H  
 VGRQETGVRRWAFILCQIPSPPLTSSEFIQRFLPRELQIVRTL DHKNI IQVYEMLESADG  
 KICLVMELAEAGDVFDVLCVNGGPLPESRAKALFRQMV EAIRYCHGCGVAHRDLKCENALL  
 QGFNLKLTDFGFAKVLPKSHRELSQTF CGSTAYAAPEVLQGI PPKMLWQQQKGVSPFTHL  
 SISADCQDLLKRLLEPDMILRPSIEEVSHPWLAST

SEQ ID NO: 216\_H29974\_H  
 YSLLAEIGRGSYGVVYEAVAGRSGARVAVKKIRCDAPENVELALAEFWALTSLKRRHQNV  
 VQFEECVLQRNGLAQRM SHGNKSSQLYLRLVETSLKGERILGYAEPCYLWFMFCEGG  
 DLNQYVLSRRPDPATNKSFMLQLTSAIAFLHKNHIVHRDLKPDNILITERSGTPILKVAD  
 FGLSKVCAGLAPRGKEGNQDNKNVNVN KYWLSSACGSDFYMAPEVWEGHYTAKADIFALG  
 IIIWAMIERITFIDSETKELLGTIYIKQGT EIVPVGEALLENPKMELHIPQKRRTSMSEG  
 IKQLLKDMLAANPQDRPD AFELETRMDQVTCAA

SEQ ID NO: 217\_AA498104\_M H29974\_M  
 PLLLP PPPAAMETGKENGARRGTS PERKRRSPVQ RVLCEKLRPAAQAMDPAGAEVPGEA  
 FLARRRPDGGGDV PARPRYSLLAEIGRGSYGVVYEAVAGRSGARVAVKKIRCDAPENVE  
 LALAEFWALTSLKRRHQNI VQFEECVLQRNGLAQRM SHGNKNSQLYLRLVETSLKGERIL  
 GYAEPCYLWFMFCEGGDLNQYVLSRRPDPATNKSFMLQLTSAIAFLHKNHIVHRDLK  
 PDNILITERSGTPILKVAD FGLSKVCAGLAPRGKEGNQDNKNVNVN KYWLSSACGSDFYM  
 APEVWEGHYTAKADIFALG IIIWAMIERITFIDSETKELLGTIYIKQGT EIVPVGEALLE  
 NPKMELHIPQKRRTSMSEGVKQLLKDMLAANPQDRPD AFELETRMDQVTCAA

SEQ ID NO: 218\_AA215311\_H  
 MVSSQPKYDLIREVGRGSYGVVYEAVIRKTSARVAVKKIRCHAPENVELALREFWALSSI  
 KSQHPNVIHLEECILQKDMVQKMSHGSNSSLYLQLVETSLKGEIAFDPRSAYYLWFMVD  
 FCDGGDMNEYLLSRKPNRKTNTS FMLQLSSALAF LHKNI IHRDLKPDNILISQTRLDT  
 DLEPTLKVADFGLSKVCSASGQNPEEPVSVNKCFLSTACGTFYMAPEVWEGHYTAKADI  
 FALG IIIWAMLERITFIDTETKELLGSYVKQGT EIVPVGEALLENPKMELLI PVKKKSM  
 NGRMKQLIKEMLAANPQDRPD AFELELRVLVQIAFKDSSWET

SEQ ID NO: 219\_AA018361\_H  
 MRAAFPAGGAGGSVEPPSARPAPQ PAGTAARSEEAPARAQAAGMAGPGWGPRLDGFILT  
 ERLGSGTYATVYKAYAKD TREVVAIKCVAKSLNKASVENLLTEIEILKGIRPHIVQL  
 KDFQWSDNIYLIMEFCAGGDL SRFIHTRILPEKVARVFMQQLASALQFLHERNISHLD  
 LKPQNILLSSLEKPHLKLADFGFAQH MSPWDEKHVLRGSPLYMAPEMVCQRQYDARVDLW  
 SMGVILYEALFGQPPFASRSFSELEEKIRSNRVIELPLRPLLSRDCRDLQRLLERDPSR  
 RISFQDFFAHPWVDLEHMPSGESLGRATALVVQAVKKDQEGDSAAALS LYCKALDFFVPA

## FIGURE 1X

LHYEVDAQRKEAIKAKVGQYVSRAEELKAIVSSSNQALLRQGTSARDLLREMARKPRLL  
AALEVASAAMAKEEAAGGEQDALDLYQHSLGELLLLLRSRPRAGGGSCFTLRFRTSWPELN  
T

SEQ ID NO: 220\_AA311714\_H  
MENFILYEEIGRGSKTVVYKGRRKGTINFVAILCTDKCRRPEITNWVRLTREIKHKNIVT  
FHEWYETSNHLWLXENLPEDVVREFGIDLISGLHHLHKLGLFCDISPRKILLEGPGTL  
KFSNFCIAKVEGENLEEFALVAAEEGGGNGENVLKKSMKSRVKGSPVYTAPENVVRGAD  
FSISSDLWSLGLLYEMFSGKPPFFSESSELTEKILCEDPLPPIPKDSSRPKASSDFIN  
LLDGLLQDRDPQKRLTWTRLLQHSFWKKAFAAGADQESSVEDLSLSRNTMECSGPQDSKELL  
QNSQSRQAKGHKSGQPLGHSFRLNPTEFRPKSTLEGQLNESMFLSSRPTPTSTAVEV  
SPGEDMTHCSPQKTSPLTKITSGHLSQQDLESQMRELIYTDSDLVVTPIIDNPKIMKQPP  
VKFDAKILHLPTYSDKLLFLKDQDWNDFLQQVCSQIDSTEKSMGASRAKLNLLCYLCVV  
AGHQEVATRLLHSPLFQLLIQHLRIAPNWDIRAKVAHVIGLLASHTTELQENTPVVETTS  
SIGIGILNCLVQHSTPVPRQCLVYV

SEQ ID NO: 221\_SGK384\_H  
SLAHVLRARQILTEPEVRDYLRLGLVSGRLYLHQRCILHR

SEQ ID NO: 222\_AA210451\_M SGK384\_M  
MGQQHGTRNGLTHRELPRGVGLLLAMALMNVALYLCLDQLFISPRGSTADSRRCPPGYFR  
MGRMRNCSRWLSCEELRTEVRQLKRVGEGAVKRVFLSEWKEHKVALSRLRLEMKEDFLH  
GLQMLKSLQSEHVVTLVGYCEEDGTILTEYHPLGSLSNLEETLNLSKYQDVNTWQHRLQL  
AMEYVSIINYLHHSPLGTRVMCDNDLPKTLQYLLTSNFSIVANDLDALPLVDHDSGVL  
IKCGHRELHGDFVAPEQLWPYGEDTPFQDDLMPSYNEKVDIWKIPDVSSFLGHVEGSDM  
VRFHLDIHKACKSQIPAERPTAQNVLDAYQRVFHSRLRDTVMSQTKEML

SEQ ID NO: 223\_SGK071\_2\_H  
EVVAVQMMVECMDDHYASQALEELMPLLKLRAHISVYQELFITWNGEISSLYLCLVMEF  
NELSFQEVIEDKRKAKKIIDSEWMQNVLGQVLDALAYLHHLDIHRNLKPSNIILISSDH  
CKLQDLSSNVMLTDKAKWNIIRAEEDPFRKSWMAPEALNFSFSQKSDIWSLGCIIIDMTSC  
SFMGTEAMHLRKSRLRQSPGSLKAVLKTMEEKQIPDVETFRNLLPLMLQIDPSDRITIKD  
VVHITFLRGSFKSSCVSLTLHRQMPASITDMLLEGNVASILGDAGDTKGERALKLLSMA  
LASYCLVPEGSFLMPLALLMHMDQWLSCDQDRVPGKRDFAKGLGKLLGPIPKGLPWPP  
ELVEVVVTTMELHDRVLDVQLCACSLLLHLLGQALVHHPEAKAPCNQAITSTLLSALQSH  
PEEEPLLVMVYSLLAITTTQESSESLSEELQAGLLEHILEHLNSSLERSDVCASGLGLLW  
ALLLDDPILALQRPRKKRAPNHGKPGKPNPASTQSIIVNKAPLEKVPDLISQVLATYPA  
DGEMAEASCQVFWLLSLLGCIKEQQFEQVALLLQSIIRLCQDRALLVNNAYRGLASLVKV  
SELAAPKVVVQEEGGSGLSLIKETYQLHRDDPEVVENVGMMLLVHLASYEELPELVSSSM  
KALLQEIKERFTSSSLVSDSSAFSKPGLPPGGSPQLGCTTSGGLE

SEQ ID NO: 224\_AA118352\_M SGK071\_M  
EEDPCQKSWMAPEALKFSFSTKSDIWSLGCIIIDMATCSFLNDTEAMQLRKAIRHHPGSL  
KPILKTMEEKQIPGTDVYYLLLPFMLHINPSDLRAIKDVMQVTFMSNSFKSSSVANMQR  
QKVPIFITDVLLGNMANILGSWLCASFVNDNRHCDSGIGSQRLGFDQFSVSWTEHPLKD  
VMQNFSSRPEVQLRAINKLLTMPEDQLGLPWPTELLEVISI IKQHGRILDILLSTCSLL  
LRVLGQALAKDPEAEIPRSSLIISFLMDTLRSHPNSERLVNVVYNVLAIISSQGQISEEL  
EEEGFLQLAQENLEHFQEDRDICLSILSLLWSLLVDVVTVDKEPLEQLSGMVTWVLATHP  
EDVEIAEAGCAVLWLLSLLGCIKESQFEQVVVLLLSIQLCPGRVLLVNNAFRGLASLAK

## FIGURE 1Y

VSELVAFRIVVLEEGSSGLHLIQDIYKLYKDDPEVVENLCMLLAHLTSYKEILPEMESGG  
IKDLVQVIRGRFTSSLELISYADEILQVLEANAQPGQLQEDQLEPPAGQEAPLQGEPLFRP

SEQ ID NO: 225\_018653.9\_H

GRGRGAGHARGLGRGPAGRRAPPRSLSRPGPGPSRAGPAGRGEGSDAAPAGGSGRGFL  
RLLPAGLRPQRALRSGSEPPRPGQSPEPSPAPGAGRRGGRGELARQIRARYEEVQRYSRG  
GPGPGAGRPERRRLMDLAPGGPGLPRPRPPWARPLSDGAPGWPPAPGPGSPGPGPRLGCA  
ALRNVSGAQYMGSGYTKAVYRVRLPGGAVALKAVDFSGHDLGSCVREFGVRRGCYRLAA  
HKLLKEMVLLERLRHPNVLQLYGYCYQDSEDI PDTLTTI TELGAPVEMIQLLQTSWEDRF  
RICLSLGRLLHHLAHSPLGSVTLDFRPRQFVLVDGELKVTDLDDARVEETPCAGSTDCI  
LEFPARNFTLPCSAQGWCEGMNEKRNLNAYRFFFTYLLPHSAPPSLRPLLDSIVNATGE  
LAWGVDETLAQLEKVLHLYRSGQYLQNSTASSSTEYQCI PDSTI PQEDYRCWPSYHHGSC  
LLSVFNLAEAVDVCESHAQCRAFVVTNQT TWTGRQLVFFKTGWSQVVPDPNKTTYVKASG

SEQ ID NO: 226\_AA396601\_M

TRPGCAALRNVSGAQYVVGSGYTKAVYRVRLPGGAVALKAVDFSGHDLGSCVREFGARRG  
CYRLAAHKLLKEMVLLERLRHPNVLQLYGYCYQDSEGI PDTLTTI TELGAPVEMIQLLQTS  
SWEDRFRI CLSLGRLLHHLAHSPLGSVTLDFRPRQFVLVNGELKVTDLDDARVEETPCT  
SSADCTLEFPARNFSLPCSAQGWCEGMNEKRNLNAYRFFFTYLLPHSAPPSLRPLLDSI  
VNATGELAWGVDETLAQLETAHLFRSGQYLQNSTSSRAEYQRI PDSAITQEDYRCWPSY  
HHGGCLLSVFNLAEAIDVCESHAQCRAFVVTNQT TWTGRKL VFFKTGWNQVVPDAGKTTY  
VKAPG

SEQ ID NO: 227\_VRK3\_H

MISFCPCGKSIQA AFKFCPYCGNSLPVEEHVGSQTFVNP HVSSFQGSKRGLNSSFETSP  
KKVKWSSTVTSRPLSLFSDGDSSESEDTLSSSSERSKSGSRPPTPKSSPQKTRKSPQVTR  
GSPQKTS CSPQKTRQSPQTLKRSRVTT SLEALPTGTVLTDKSGRQWKLKSFQTRDNQGIL  
YEAAPTSTLTCDSGPQKQKFSCLKDAKDGR LFNEQNFFQRAAKPLQVNKWKLYSTPLLA  
IPTCMGFGVHQDKYRFLVLP SLGRSLQ SALDVSPKHVLSERSVLQVACRLLDAL EFLHEN  
EYVHGNTAENIFVDPEDQSQVTLAGYGFAFRYCPSGKHVAYVEGSRSPHEGDLEFI SMD  
LHKGCGPSRRSDLQSLGYCMLKWLYGFLPWTNCLPNTEDIMKQKQKFVDKPGPFVGP CGH  
WIRPSETLQKYLKVVMA LT YE EKPPYAMLRNNLEALLQDLRVSPYDPIGLPMVP

SEQ ID NO: 228\_S71575\_M VRK3\_M

IPTCIGFGIHQDKYRFLVFP SLGRSLQ SALDDNPKHVVSERCVLQVACRLLDAL EYLHEN  
EYVHGNTAENFVN PEDLSQVTLVG YGFTYRYCPGGKHVAYKEGSRSPHDGDLEFI SMD  
LHKGCGPSRRSDLQTLGYCMLKWLYGSLPWTNCLPNT EKITRQKQKYLDSPERLVGLCGR  
WNKASETLREYLKVVMA LN YE EKPPYATLRNSLEALLQDMRVSPYDPLDLQMPV

SEQ ID NO: 229\_AA45427\_H

MGHALCVCSRGTVI IDNKRYLFIQKLGE GGF SYVDLVEGLHDGHFYALKRI LCHEQQDRE  
EAQREADMHRLFNHPN IRLVAYCLRERGAKEAWLLLPFFKRGTLWNEIERLKDKGNFL  
TEDQILWLLLGICRGLEAIHAKGYAHRDLKPTN ILLGDEGQPVLM DLGSMNQACIHVEGS  
RQALTQDWAAQRCTISYRAPELFSVQSHCVI DERTDVWSLGC VLYAMMFEGGPYDMVFQ  
KGDSVALAVQNQLSIPQSPRHSSALRQLLNSMMTVDPHQRP H I P L L L S Q L E A L Q P P A P G Q  
HTTQI

SEQ ID NO: 230\_H05721\_H

MAVRQALGRGLQLGRALLRFTGKPGRAYGLGRPGPAAGCVRGERPGWAAGPGAEP RRVG  
LGLPNRLRFFRQSVAGLAARLQRQFVVRAGCAGPCGRAVFLAFGLGLGLIEEKQAESRR

## FIGURE 1Z

AVSACQEIQAIFTQKSKPGPDPLDTRRLQGFRLEEYLIGQSIGKGCSAAVYEATMPTLPQ  
 NLEVTKSTGLLPGRGPGTSAPGEGQERAPGAPAFPLAIKMMWNI SAGSSSEAILNTMSQE  
 LVPASRVALAGEYGAVTYRKS KRGPQKLAPHPN IIRVLRAFTSSVPLLP GALVDYDPDVL P  
 SRLHPEGLGHGRTLFLVMKNYPCTLRQYLCVNTPSRLAAMMLLQLLEGVDHLVQQGIAH  
 RDLKSDNILVELDPDGPWLVIADFGCCLADESIGLQLPFSSWYVDRGNGCLMAPEVST  
 ARPGPRAVIDYSKADAWAVGAIAYEIFGLVNPFGYQGGKAHLESRSYQEAQLPALPESVPP  
 DVRQLVRALLQREASKRPSARVAANVLHLSLWGEHILALKNLKLDKMGVWLLQQAATLL  
 ANRLTEKCCVETKMKMLFLANLECETLCQAALLLCSWRAAL

SEQ ID NO: 231\_AI086865\_H  
 MEKYERIRVVGRGAFGI VHLCLRKADQKLVI I KQIPVEQMTKEERQAAQNECQVLKLLNH  
 PNVEYYENFLEDKALMIAMEYAPGGTLAEFIQKRCNSLLEEETILHFFVQIILLALHHVH  
 THLILHRDLKTQNILLDKHRMVVKIGDFGISKILSSKSTPCYISPCEGKPYNQKSDIW  
 ALGCVLYELASLKRAFEAANLPALVLKIMSGTFAPISDRYSPELRQLVLSLLSLEPAQRP  
 PLSHIMAQPLCIRALLNLHTDGREVRGPQQHREQDHQCPLQGIIMTFGSGSNGCLGHGS  
 LTDISQPTIVEALLGYEMVQQVEEALSFTLLGSAPLDQEPILLSIDLGTAHSAAVTGEEDL  
 GSGDVNRLPSWERGHLLAGVASSTDVSTFSEGDCKEPPDKCCWRHKQCTGHI IYPFASDCV  
 RHSLHLHSVNHCNCSRLKDSSSEDSSSSRGAGPTCSHVIESPCFELTPEEEHVERFRYGW  
 CKSYRPVSVAVIHHPLYHECGADDLNXXKRKRKRKRKRKSKPPIPTQVGPATASPDLTGSMAT  
 GTPDSTAPITIWRSSEPTGKGQGSKVIKKVKKKKEKEKDKEEMDEKAKLKKKAKKGQLTK  
 KKSPPVKLEPSPDPVSRSLARQLARMESSPESREELESEDSYNGRGQGELSSSEDI VESS  
 SPRKRENTVQAKKTGAKPSQARKVNRKSPPGSNPNLS

SEQ ID NO: 232\_AA836348\_H  
 MSVLGEYERHCDSINSDFGSESGCGDSSPGPSASQGPAGGGAAEQEELHYIPIRVLGR  
 GAFGEATLYRRTEDDSL VVWKEVDLTRLSEKERRDALNEI VILALLQHDNI IAYYNHFM D  
 NTTLLIELEYCNGGNLYDKILRQKDKLFEEEMVVWYLFQIVSAVSCIHKAGILHRDIKTL  
 NIFLTKANLIKLG DYGLAKKLNSEYSMAETLVGTPPYMSPELCQGVKYNFKSDI WAVGCV  
 IFELLTLKRTFDATNPLNLCVKI VQGI RAMEVDSSQYSLELIQMVHSCLDQDPEQRPTAD  
 ELLDRPLLRRRRSSSTVTEAPIAVVTSTRTSEVYVWGGGKSTPQKLDVIKSGCSARQVCAG  
 NTHFAVVTVKEKELYTWVNMQGGTKLHGQLGHGDKASYRQPKHVEKLQGKAIRQVSCGDDF  
 TVCVTDEGQLYAFGSDYYGCMGVDKVAGPEVLEPMQLNFFLSNPVEQVSCGDNHVVVLTR  
 NKEVYSWGCGEYGRGLDSEEDYYTPQKVDVPKALI I VAVQCGCDGTFLLTQSGKVLACG  
 LNEFNKLGLNQCMSGI INHEAYHEVPYTTSFTLAKQLSFYKIRTIAPGKTHTA AIDERGR  
 LLTFGCNKCGQLGVGNYKKRLGINLLGGPLGGKQVIRVSCGDEFTIATDEKVLNSKTI R  
 SNSSGLSIGTVFQSSSPGGGGGGGGGEEEDSQQESETPDPSSGGFRGTMEADRGMEGLISP  
 TEAMGNSNGASSSCPGLRKELENAEFIPMPDPSPLSAAFSESEKDTLPYEELQGLKVA  
 SEAPLEHKPQVEASVTELF AFESQLVTSAESCSNLCWEGNTTDS SCVCVQLSAGG

SEQ ID NO: 233\_R86668\_H, MKK6\_H  
 MNLLLSYRDVQDYSAI IELVETLQALPTCDVAEQHNVC FHYTFALNRRNRPGDRAKALSV  
 LLPLVQLEGSVAPDLYCMCGRIYKDMFFSSGFQDAGHREQAYHWYRKAFDVEPSLHSGIN  
 AAVLLIAAGQHFEDSKELRLIGMKLGCLLARKGCVEKMQYYWDVG FYLGAQILANDPTQV  
 VLA AEQLYKLNAPIWYLVSMETFLLYQHFRPTPEPPGGPPRAHFWLHFL LQSCQPFKT  
 ACAQGDQCLVLVLEMNKVLLPAKLEVRGTDVPSTVTL SLLPETQDIPSSWTFPVASICG  
 VSASKRDERCCFLYALPPAQDVQLCFPSVGHQCWFGLIQAWVTNPDSTAPAEAEAGAGE  
 MLEFDYEYTETGERLVLGKGTYG VVYAGRDRHTRVRIAIKEI PERDSRFSQPLHEEIALH  
 RRLRHKNIVRYLGSASQGGYLKIFMEEVPGGSLSSLLRSVWGPLKDNESTISFYTRQILQ  
 GLGYLHDNHI VHRDIKGD NVLINTFSGLLKISDFGTSKRLAGITPCTETFTGT LQYMAPE  
 IIDQGPRGYGKAADIWSLGCTVIEMATGRPPFHELGSQAAMFQVGMVKVHPPMPSSLSA



## FIGURE 1AA

EAQAFLLRTFEPDPRLRASAQTLLGDPFLQPGKRSRSPSSPRHAPRPSDAPSASPTPSAN  
STTQSQTFFPCPQAPSQHPPSPPKRCLSYGGTSQLRVPEEPAAEPPASPEESSGLSLLHQE  
SKRRAMLA AVL EQELPALAENLHQEQKQEQGARLGRNHVEELLRCLGAHIHTPNRRQLAQ  
ELRALQGRLRAQGLGPALLHRPLFAFPDAVKQILRKRQIRPHWMFVLDSLLSRVRAALG  
VLGPEVEKEAVSPRSEELSNEGDSQQSPGQQSPLPVEPEQGPAPLMVQLSLLRAETDRLR  
EILAGKEREYQALVQRALQRLNEEARTYVLAPEPPTALSTDQGLVQWLQELNVDSGTIQM  
LLNHSFTLHTLLTYATRDDLITYTRIRGGMVCRIWRILAQRAGSTPVTSGP

SEQ ID NO: 234\_PAK6\_H

MFGKKKKKIEISGPSNFEHRVHTGFDPQEQKFTGLPQQWHSLLADTANRPKPMVDPSCIT  
PIQLAPMKTIVRGNKPKETSINGLLEDFDNISVTRSNSLRKESPPTPDQGASSHGPGHA  
EENGFITFSQYSSSEDTTADYTTEKYREKSLYGGDLDPYYRGSHAAKQNGHVMKMKHGEA  
YYSEVKPLKSDFARFSADYHSHLDSLSKPSEYSDLKWEYQRASSSSPLDYSFQFTPSRTA  
GTSGCSKESLAYSESEWGPSLDDYDRRPKSSYLNQTSPOPTMRQRSRSGSGLQEPMPFPG  
ASAFKTHPQGHSYNSYTYPRLSEPTMCIPKVDYDRAQMVLSPLSGSDTYPRGPAKL PQS  
QSKSGYSSSSHQYPSGYHKATLYHHPSLQSSSQYISTASYLSSLSLSSSTYPPPSWGSSS  
DQQPSRVSHQFRAALQLVSPGDPREYLANFIKIGEGSTGIVCIATEKHTGKQVAVKKM  
DLRKQQRRELLFNEVVIMRDYHHDNVVDMYSSYLVGDELWVMEFLEGGALTDIVTHTRM  
NEEQIATVCLSVLRALSYLHNQGV IHRDIKSDSILLTSDGRIKLSDFGCAQVSKEVPKR  
KSLVGTPYWMapevisrlpygtevdiwslgimviemidgepppyfnepplqamrrirdslp  
PRVKDLHKVSSVLRGFLDLMLVREPSQRATAQELLGHPFLKLAGPPSCIVPLMRQYRHH

SEQ ID NO: 235\_SURTK106\_H

MNDRNEIQMEAKLQSLTIIAQEILCRFFITLRRHARFLLTKLGRQGMARSGITHSCAVCI  
LCGPSREGDSPVAMGMTRMLLECSLSDKLCVIEKQYEVII VPTLLVTIFLILLGVILWL  
FIREQRTQQQRSGPQGIAPVPPPRDLSWEAGHGGNVALPLKETSVENFLGATTPALAKLQ  
VPREQLSEVLEQICSGSCGPIFRANMNTGDPSKPKSVILKALKEPAGLHEVQDFLGRIQF  
HQYLKGKHNVLQLEGCCTEKLPLYMVLEDVAQGDLLGFLWTCRRDVMTMDGLLYDLTEKQ  
VYHIGKQVLLALEFLQEKHLFHGDVAARNILMQSDLTAKLCGLGLAYEVYTRGAISSTQT  
IPLKWLAPERLLL RPASIRADVWSFGILLYEMVTLGAPPYPEVPPTSILEHLQRRKIMKR  
PSSCTHTMYSIMKSCWRWREADRPSPRELRLRLEAAIKTADDEAVLQVPELVPELYAAV  
AGIRVESLFYNY SML

SEQ ID NO: 236\_AA098024\_M

LQEKHLFHGDVAARNILIQSDLTPKLCHLGLAYEVHAHGAISSARSSTIPLKWLAPERLL  
LRPASIRGDIWSFGILLYEMVTLGAPPYPEVPPTSILQYLQRRKIMKRPSSCSHAMYNIM  
KCCWRWSEDSRPLLQVLLQRLQLEAASRSADDKAVLQVPELVPELYADVAGIRAESISYSF  
SVL

SEQ ID NO: 237\_SGK2ALPHA\_H

MNSSPAGTSPQPSRANGNINLGPSANPNAQPTDFDLKVIKGNYGKVLLAKRKSDGAF  
YAVKVLQKKSILKKKEQSHIMAERSVLLKNVRHPFLVGLRYSFQTPEKLYFVL DYVNGGE  
LFFHLQRRERRFLEPRARFYAAEVASAIGYLHSLNIIYRDLKPENILLDCQGHVVLTD FGL  
CKEGVEPEDTTSTFCGTPEYLAPEVLRKEPYDRAVDWWCLGAVLYEMLHGLPPFYSQDVS  
QMYENILHQPLQIPGGRTVAACDLLQSLHDKDQORQLGSKADFLEIKNHVFFSPINWDDL  
YHKRLTPPFNPNTGPADLKHFDPEFTQEAVSKSIGCTPDTVASSSGASSAFLGFSYAPE  
DDDILDC

## FIGURE 1BB

SEQ ID NO: 238\_CCRK\_H  
MDQYCILGRIGEGAHVFKAKHVETGEIIALKKVALRRLEDGFPNQALREIKALQEMED  
NQYVVLKAVFPHGGLVLAFFMLSDLAEVVRHAQRPLAQAQVKSQMLLKGVAFCHA  
NNIVHRDLKPANLLISASGQLKIADFGRLARVFSPDGSRLYTHQVATRSVGCIMGELLNGS  
PLFPGKNDIEQLCYVLRILGTPNPQVWPELTELDPYDKISFKEQVPMPLLEVLDPVSPQA  
LDLLGQFLLYPPHQRIAASKALLHQYFFTAPLPAHPSELPIPQRLGGPAPKAHPGPPH  
DFHVDRLPLEGVAVEPRADSALHPGGVRSWPWSRLPAPQDHSVHLFLCHLPGFTLQGLPMA  
TVGPHHTLPLSPCEGWSRGRGHVPSQEYENIQSSRGDSWPVLGEPYLLCATDVPRTVSS  
AASQGLHMQNDACLGAASPECCLLVKEKCRE

SEQ ID NO: 239\_TESK2\_H  
MDRSKRNSIAGFPFRVERLEEFEGGGGEGNVSVQVGRVWPSSYRALISAFSRLTRLDDFT  
CEKIGSGFFSEVFKVRHRASGQVMALKMNTLSSNRANMLKEVQLMNRLSHPNILRYNSG  
NLEQLLDSNLHLPWTVRVKLAYDIAVGLSYLHFKGIFHRDLTSKNCLIKRDENGYSAVVA  
DFGLAEKIPDVSMGSEKLAVVGSPPFWMAPEVLRDEPYNEKADVFSYGIILCEIIARIQAD  
PDYLPRTENFGLDYDAFQHMVGDCPPDFLQLTFNCCNMDPKLRPSFVEIGKTLLEEILSRL  
QEEQERDRKLQPTARGLLEKAPGVKRLSSLDDKI PHKSPCPRRTIWLRSQSDIFSRKP  
PRTVSVLDPYYRPRDGAARTPKVNPFSARQDLMGKIKFFDLPSKSVISLVFDLDAPGPG  
TMPLADWQEPLAPPIRRWRSPLGSPFLHQEACPFVGREESLSDGPPRLSSLKYRVKEI  
PPFRASALPAAQAHEAMDCSILQEENGFGSRPQGTSPCPAGASEEMEVEERPAGSTPATF  
STSGIGLQTQKQDG

FIGURE 2A

SEQ ID NO: 1\_X69117\_H BARK2\_H

ATGGCGGACCTGGAGGCCGTGCTGGCCGATGTCAGTTACCTGATGGCCATGGAGAAGAGC  
AAGGCGACCCCGGCCGCCGCCAGCAAGAGGATCGTCCTGCCGGAGCCCAGTATCCGG  
AGTGTGATGCAGAAGTACCTTGACAGAGAGAAATGAAATAACCTTTGACAAGATTTTCAAT  
CAGAAAATTGGTTTCTTGCTATTTAAAGATTTTGTGTTGAATGAAATTAATGAAGCTGTA  
CCTCAGGTGAAGTTTTATGAAGAGATAAAGGAATATGAAAACTTGATAATGAGGAAGAC  
CGCCTTTGCAGAAGTCGACAAATTTATGATGCCTACATCATGAAGGAACTTCTTTCCTGT  
TCACATCCTTTCTCAAAGCAAGCTGTAGAACACGTACAAAGTCATTTATCCAAGAAACAA  
GTGACATCAACTCTTTTTCAGCCATACATAGAAGAAATTTGTGAAAGCCTTCGAGGTGAC  
ATTTTTCAAAAATTTATGGAAAGTGACAAGTTCCTAGATTTTGTGAGTGGAAAAACGTT  
GAATTAAATATCCATTTGACCATGAATGAGTTCAGTGTGCATAGGATTATTGGACGAGGA  
GGATTCGGGGAAGTTTATGGTTGCAGGAAAGCAGACACTGGAAAAATGTATGCAATGAAA  
TGCTTAGATAAGAAGAGGATCAAAATGAAACAAGGAGAAACATTAGCTTTAAATGAAAGA  
ATCATGTTGTCTCTGTGTCAGCACAGGAGACTGTCCTTTCATTGTATGTATGACCTATGCC  
TTCCATACCCAGATAAACTCTGCTTCATCCTGGATCTGATGAACGGGGGCGATTTGCAC  
TACCACCTTTCAACACGGGTGTGTTCTCTGAGAAGGAGATGCGGTTTTATGCCACTGAA  
ATCATTCTGGGTCTGGAACACGTGCACAATCGGTTTGTGTTGTCTACAGAGATTTGAAGCCA  
GCAAAATATTCTCTTGATGAACATGGACACGCAAGAATATCAGATCTTGGTCTTGCCTGC  
GATTTTTCAAAAAGAAGCCTCATGCGAGTGTGGCACCCTATGGGTACATGGCTCCCGAG  
GTGCTGCAGAAGGGGACGGCCTATGACAGCAGTGGCGACTGGTCTCCCTGGGCTGCATG  
CTTTTCAAACCTTCTGAGAGGTACAGCCCTTTCAGACAAACATAAAACCAAAGACAAGCAT  
GAAATTGACCGAATGACACTCACCGTGAATGTGGAACCTCCAGACACCTTCTCTCCTGAA  
CTGAAGTCCCTTTTGGAGGGCTTGCTTCAGCGAGACGTTAGCAAGCGGCTGGGCTGTCAC  
GGAGGCGGCTCACAGGAAGTAAAAGAGCACAGCTTTTTCAAAGGTGTTGACTGGCAGCAT  
GTCTACTTACAAAAGTACCCACCACCCTTGATTCTCTCCCGGGGAGAAGTCAATGCTGCT  
GATGCCTTTGATATTGGCTCATTTGATGAAGAGGATACCAAAGGGATTAAGCTACTTGAT  
TGCGACCAAGAACTCTACAAGAACTTCCCTTTGGTCATCTCTGAACGCTGGCAGCAAGAA  
GTAACGGAAACAGTTTATGAAGCAGTAAATGCAGACACAGATAAAATCGAGGCCAGGAAG  
AGAGCTAAAAATAAGCAACTTGGCCACGAAGAAGATTACGCTCTGGGGAAGGACTGTATT  
ATGCACGGGTACATGCTGAAACTGGGAAACCCATTTCTGACTCAGTGGCAGCGTCGCTAT  
TTTTACCTCTTTCCAAATAGACTTGAATGGAGAGGAGAGGGAGAGTCCCGGCAAAATTTA  
CTGACAATGGAACAGATTCTCTCTGTGGAAGAACTCAAATTAAGACAAAAATGCATT  
TTGTTGAGAAATAAAGGAGGGAAACAATTTGTCTTGCAATGTGAGAGTGATCCAGAGTTT  
GTGCAGTGGAAGAAAGAGTTGAACGAAACCTTCAAGGAGGCCAGCGGCTATTGCGTCGT  
GCCCCGAAGTTCTCTCAACAAACCTCGGTACGTGAGCTCCCAAAGCCATCCCTC  
TGTCACAGGAACAGCAACGGCCTCTGA

SEQ ID NO: 2\_AA144574\_M BARK2\_M

CTGCTTCGTAGTCTACAGAGACCTGAAGCCTGCGAACATCCTCCTAGATGAATATGGGCA  
CGTGAGGATATCGGATCTCGGCCTTGCTGTGATTTCTCCAAAAGAAGCCTCATGCCAG  
CGTGGGCACCCATGGGTACATGGCTCCCGAGGTGTTGCAGAAGGGAACGTGCTATGACAG  
CAGCGCCGACTGGTCTCCCTGGGCTGTATGCTCTTCAAACCTTCTGCGGGGCCACAGCCC  
CTTCAGGCAGCATAAAACCAAAGACAAGCATGAGATAGACCGAATGACCCTGACCGTGAA  
CGTGCAGCTTCCAGATGCCTTCTCCCCTGAGCTGAGGTCCCTCTTAGAGGGTTTGCTCCA  
GCGGGACGTGAGCCAGCGGCTGGGCTGCGGAGGAGGAGGGGCACGAGAGTTGAAGGAGCA  
CATCTTCTTCAAGGGCATTGACTGGCAGCATGTGTACTTACGGAAGTACCCGCCACCCCT  
AATCCCTCCTCGGGGAGAGGTCAACGCTGCAGATGCCTTCGATATCGGCTCCTTCGATGA  
GGAAGACACCAAAGGCATTAAGCTGTTGGACTGTGACCAGGACCTCTATAAGAACTTCCC  
ACTGGTGATCTCCGAGCGCTGGCAGCAAGAAGTGGTGGAGACCATCTATGACGCCGTCAA  
TGCTGATACTGATAAAATCGAGGCCAGGAAGAAGGCTAAAAATAAGCAACTTGGTCAAGA

## FIGURE 2B

GGAAGATTACGCTATGGGGAAGGACTGCATCATGCACGGGTACATGCTGAAGCTGGGGAA  
CCCCTTTCTCACACAGTGGCAAAGACGCTATTTTACCTGTTCCCAACAGACTGGAGTG  
GAGAGGAGAGGGCGAGTCTCGGCAAAGTCTACTGACCATGGAACAGATCATGTCTGTGGA  
GGAGACCCAGATTAAAGACAGAAAGTGCATCTTACTCAGGATAAAGGGAGGGAAGCAATT  
TGTCTTGCAATGTGAGAGTGACCCCGAGTTTGCACAGTGGCTGAAGGAGCTGACCTGCAC  
CTTCAATGAGGCCCAGAGACTGCTGCGCCGTGCCCCCAAATTCCTCAACAAACCACGGGC  
CGCCATCCTGGAGTTCTCCAAGCCACCACTGTGTACAGAAATAGCAGCGGCCTCTGAAC  
CACAGAGCAGCGGGCCTGAAGGAGGGGCCCCAGCTCTTCAGCCCAGGAGTGGAACGAAG  
CCACGGGGAACCGTGTGGGGCTAAGACACAGTGTCTTCTGAGCACTGACGGGGCTGCTCCA  
AGCCGAGGAGGCTCAGGACACCAGGGCGGCCTTCTGGGAGCTGGGACATCCTCGGGGCTG  
TCCTATCCACACTCGAAATTACTGAAGAAGCAGAGGCATTCTGCTGTG

SEQ ID NO: 3\_AA826850\_H

GAAGAGGATGGGCTCGTCCATGTCGGCGGCCACCGCGGGAGGCGGCTGTTTGACGACAA  
GGAGGACGTGAACTTCGACCACTTCCAGATCCTTCGGGCCATTGGGAAGGGCAGCTTTGG  
CAAGGTGTGCATTGTGCAGAAGCGGGACACGGAGAAGATGTACGCCATGAAGTACATGAA  
CAAGCAGCAGTGCATCGAGCGCGACGAGGTCCGCAACGTCTTCCGGGAGCTGGAGATCCT  
GCAGGAGATCGAGCACGTCTTCTGGTGAACCTCTGGTACTCCTTCCAGGACGAGGAGGA  
CATGTTTCATGGTCGTGGACCTGCTACTGGGCGGGGACCTGCGCTACCACCTGCAGCAGAA  
CGTGACGTTCTCCGAGGACACGGTGAGGCTGTACATCTGCGAGATGGCACTGGCTCTGGA  
CTACCTGCGCGGCCAGCACATCATCCACAGAGATGTCAAGCCTGACAACATTCTCCTGGA  
TGAGAGAGGACATGCACACCTGACCGACTTCAACATTGCCACCATCATCAAGGACGGGGA  
GCGGGCGACGGCATTAGCAGGCACCAAGCCGTACATGGCTCCGGAGATCTTCCAXTCTTT  
TGTCAACGGCGGGACCGGCTACTCCTTCGAGGTGGACTGGTGGTGGTGGGGGTGATGGC  
CTATGAGCTGCTGCGAGGATGGAGGCCCTATGACATCCACTCCAGCAACGCCGTGGAGTC  
CCTGGTGCAGCTGTTTCAGCACCGTGAGCGTCCAGTATGTCCCCACGTGGTCCAAGGAGAT  
GGTGGCCTTGCTGCGGAAGCTCCTCACTGTGAACCCCGAGCACCGGCTCTCCAGCCTCCA  
GGACGTGCAGGCAGCCCCGGCGCTGGCCGGCGTGCTGTGGGACCACCTGAGCGAGAAGAG  
GGTGGAGCCGGGCTTCGTGCCCAACAAAGGCCGTCTGCACTGCGACCCACCTTTGAGCT  
GGAGGAGATGATCCTGGAGTCCAGGCCCTGCACAAGAAGAAGAAGCGCCTGGCCAAGAA  
CAAGTCCCGGGACAACAGCAGGGACAGCTCCAGTCCGAGAATGACTATCTTCAAGACTG  
CCTCGATGCCATCCAGCAAGACTTCGTGATTTTTTAACAGAGAAAAGCTGAAGAGGAGCCA  
GGACCTCCCGAGGGAGCCTCTCCCCGCCCTGAGTCCAGGGATGCTGCGGAGCCTGTGGA  
GGACGAGGCGGAACGCTCCGCCCTGCCCATGTGCGGCCCATTTGCCCCCTCGGCCGGGAG  
CGGCTAGGCCGGGATGCCCGTGGTCTCACCCCTTGAGCTGCTTTGGAGACTCGGCTGCC  
AGAGGGAGGGCCATGGGCCGAGGCCTGGCATTACGTTCCACCCAGCCTGGCTGGCGGT  
GCCACAGTGCCCCGGACACATTTACACCTCAGGCTCGTGGTGGTGCAGGGGACAAGAG  
GCTGTGGGTGCAGGGGACACCTGTGGAGGGCATTTCCTCGTGGGCCCCCGAGACCCGCCTA  
GATGGAGGAAGCGCTGCTGGGCGCCCTCTTACCGCTCACGGGGAGCTGGGGCCATGGATG  
GGACAGGAGTCTTTGTCCCTGCTCAGCCCGGAGGCTGTGCACGGCCCTCGTCACAAGGTG  
ACCCTTGACGACAGGCCGCGGGTGCCCCAGGCTCGGCTCAGTTCTTGGAGGTCAAGGGC  
ATGGGTTGGGGTAGTGGGTGGGGAGGTGAATGTTTTCTAGAGATTCAAAGTCTCCAGCA  
ATTTCTGTATAGTTTTTACCTCTGAGAATTACAATGTGAGAACCGCTC

SEQ ID NO: 4\_AA960957\_H

GTCCCACATCCCGCATCCGGCATCCCAGCGGGCCGGGCATGTAGCAGCGGCAGCAACGGCG  
GAATATGGGCGGGAACCACTCCCAAGCCCCCGTGTGTTGACGAGAATGAGGAAGTCAA  
CTTTGACCATTTTCAGATTCTGCGGGCCATTGGTAAAGGGAGTTTTGGAAAGGTATGCAT  
CGTGAGAAGCGAGACACTAAGAAAATGTATGCAATGAAGTACATGAACAAGCAGAAGTG  
CATCGAGAGGGATGAGGTTCCGAATGTTTTCCGGGAGCTGCAGATCATGCAAGGGCTGGA

FIGURE 2C

GCACCCCTTCCTGGTCAATCTGTGGTACTCCTTCCAGGATGAGGAGGACATGTTTCATGGT  
GGTGGACCTGCTCCTGGGAGGCGACCTGCGCTACCATCTGCAGCAGAATGTGCATTTTCAC  
AGAGGGGACTGTGAACTCTACATCTGTGAGCTGGCACTGGCCCTGGAGTATCTTCAGAG  
GTACCACATCATCCACAGAGACATCAAGCCAGACAATATCCTGCTGGATGAACACGGACA  
TGTTACATTACAGACTTCAACATAGCGACGGTAGTGAAAGGAGCAGAAAGGGCTTCCTC  
CATGGCTGGCACCAGCCCTACATGGCTCCAGAAGTATTCCAGGTGTACATGGACAGAGG  
CCCCGGATACTCGTACCCTGTGACTGGTGGTCCCTGGGCATCACAGCCTATGAGCTGCT  
GCGGGGCTGGAGGCCGTACGAAATCCACTCGGTACGCCCCATCGATGAAATCCTCAACAT  
GTTCAAGGTGGAGCGTGTCCACTACTCCTCCACGTGGTGCAAGGGGATGGTGGCCCTGCT  
GAGGAAGCTCCTGACCAAGGATCCTGAGAGCCGCGTGTCCAGCCTTCATGACATACAGAG  
CGTGGCCTACTTGGCCGACATGAACTGGGACGCGGTGTTCAAGAAGGCACTGATGCCCCG  
CTTTGTGCCCCAATAAAGGGAGGTTGAACTGCGATCCCACATTTGAGCTTGAAGAGATGAT  
TCTAGAATCCAAGCCACTTCACAAAAAGAAGAAGCGATTGGCAAAGAACAGATCCAGGGA  
TGGCACAAGGACAGCTGCCCGCTGAATGGACACCTGCAGCACTGTTTGGAGACTGTCCG  
GGAGGAATTCATCATATTCAACAGAGAGAAGCTCAGGAGGCAGCAGGGACAGGGCAGCCA  
GCTCTTGGACACCGACAGCCGAGGGGGAGGCCAGGCCCAAAGCAAGCTCCAGGACGGGTG  
CAACAACAACCTCCTCACCCACACCTGCACCCGTGGCTGCAGCAGCTGAGCCCACACTTG  
TTGCTGCTCAACAGGACTGCACTCGTCTCTGCCCTGCCACCCAGAGCCCCCTCTTTGTGC  
CCTGATGGTCCCTGTCTCACCCCTGAAAACATCAGATGCAGAAAAAGCCCTGGACTTGGA  
GCTGGGAAGCCTGGGTTCTGGTCCCATCTCCATGACTGATTACGCTGTGACCTCAGACAA  
GTCACGCCCTCTCTGTGCCTCCGTTTTCTGCATCTGCCAAAGGGTTAAACACTTCTGCC  
CCACTTCAAATTACAAGATTATGGGGAGAACCCAATTAGGTAGGAAACATGAAAAACCTT  
TGATATTTATAAAATCATTTTTACGTGCAAAATATAACCTTAATATTTGAAGTGACCCCC  
ATTCACCAAGCAATCAAACCGTCATGACTTTGCAATTTGGCACATCCTAGCTTGTTAGA  
GGGCACTTCGAAAAACACAGCCCTGACAGCAAAATAAAGGTCTGATATGTTGGCCCTT  
CTATGGAAACAACGCTGCCAAATCCTGGAGCAAAACCTGAAGTGTCTTCATGTGCATTCT  
CTGGCAGGCCACAGTCTGAGCTTGTAAGATGGTGCAGCATGCAGACCAGACTTGTCCCC  
AAGGTCTCAGCGCTGCGGTCTCACTCCTCCCTCATTTAAGAAGACTATCCTTACCTTTT  
AGTTTCAGCAGTCCCTCACCACCACCATATCCCCAGTGCTGGGATGGCACACAGGTGTCCA  
TTCAGATGAGAGTTGGGTGCTGAGCATTGGTTACTCCTGCAGAGTGTAATCAGACCCCC  
ATCCAACCTGGCCCGAAAGCCCAGACCTGCAGCAGAACTCTCCAACCTCTCTATCAGCTTTC  
AGGGTTTTCTCTCCTGGGAAGGGTGTAATAATCAGCTTGTCAGATTCTTCTTACAGAGAGT  
ATCCAATCGGTATTGGTGGAGCGGCTCCCTATTTATACAATAGGAAGCATGGGTGCTTAG  
AAAGTTTATTTTTCAGGAGGAAAATGGGTTACACAAAAAGCAAACTACATTCTGATCTGCT  
CAGGGAGAAGCTTGCCTTTGAACTGGAAGATGTTGGGATGAGCAGGGAAAGCTTAGACTT  
TGGAGTCAGGTTTGTGTTTCAAGATCCAGCCCTGCTGGCTACTAACTAACTGGGAGACCTT  
AGGCAAAGCATGCAATCGCTCTGAATGGCAGTTTCTCATTTTTTAAACAGGGATAATAAA  
ACTAATATTGCAGGGGAGTTACAGGGTTAAATAAGATCCTGTGTGTAACCCCAAGCATTG  
GATGACTCATAGAATGGCCTTTTTTGTGTCAGCATAATCGTCATCATTATTTAGATACTTTC  
TTCCTTCACTCACCCAGCAGGTGAGTTTTCTGTGCAACAAACCTGTTTAGGATTCTTCC  
AAATGTTCTTCTGGGGTCTTTGATATTTGTTTGTACATCCTGCTGAAGTTCGACTGTG  
TTTTTATTTTTTTCATCCAACCTCCATTTTTTCACTTTTTTACATGATTACTCAATCCTTGGG  
GCTGTCCATGTCATCTCTTAGATTTCTTAAAAGACATTTTAAATGTATGGTTAGGTTTTAT  
ATTTTTATTTTTTAAAAAGAAATAGTCAGTGTTTTTCTCCTTTTCAACCGAGACTATTTT  
TGGATTGTGTGCTCCTCGTCAGTTGACTTGTTTTGCACACTTTTCTTTACTTCATGTCCC  
CATCAACAACCGTCTGCTCCCCACCTCCCCCAGGAAATAAGGGGCCTGCTCCTCTCCCT  
ACTGTGACCCTGGAGGCTCTTAAGATGATGATGGTTTTTTTTTATTGGGCTGAGTTCACGA  
ATTAGGGGCAGGAGCTGGAAGTCGCCCTAGGAACACCAGATTTCCTGGTTCTGTTCAAGT  
TGGCATTCTTGTGTTGGAATAAACTATTTCTTGGACATTCCTTC

## FIGURE 2D

SEQ ID NO: 5\_TBK1\_H

TCCTGAGTCTCGAGGAGCCGCGGGAGCCCGCCGGTGGCGCGGCGGAGACCCGGCTG  
GTATAACAAGAGGATTGCCTGATCCAGCCAAGATGCAGAGCACTTCTAATCATCTGTGGC  
TTTTATCTGATATTTTAGGCCAAGGAGCTACTGCAAATGTCTTTTCGTGGAAGACATAAGA  
AAACTGGTGATTTATTTGCTATCAAAGTATTTAATAACATAAGCTTCCTTCGTCCAGTG  
ATGTTCAAATGAGAGAATTTGAAGTGTTGAAAAAACTCAATCACAAAAATATTGTCAAAT  
TATTTGCTATTGAAGAGGAGACAACAACAAGACATAAAGTACTTATTATGGAATTTTGTCT  
CATGTGGGAGTTTATACACTGTTTTAGAAAGAACCTTCTAATGCCTATGGACTACCAGAAT  
CTGAATTCCTAATTGTTTTGCGAGATGTGGTGGGTGGAATGAATCATCTACGAGAGAATG  
GTATAGTGCACCGTGATATCAAGCCAGGAAATATCATGCGTGTTATAGGGGAAGATGGAC  
AGTCTGTGTACAACTCACAGATTTTGGTGCAGCTAGAGAATTAGAAGATGATGAGCAGT  
TTGTTTCTCTGTATGGCACAGAAGAATATTTGCACCCTGATATGTATGAGAGAGCAGTGC  
TAAGAAAAGATCATCAGAAGAAATATGGAGCAACAGTTGATCTTTGGAGCATTGGGGTAA  
CATTTTACCATGCAGCTACTGGATCACTGCCATTTAGACCCTTTGAAGGGCCTCGTAGGA  
ATAAAGAAGTGATGTATAAAATAATTACAGGAAAGCCTTCTGGTGCAATATCTGGAGTAC  
AGAAAGCAGAAAATGGACCAATTGACTGGAGTGGAGACATGCCTGTTTCTTGCACTCTT  
CTCGGGGTCTTCAGGTTCTACTTACCCCTGTTCTTGCAAACATCCTTGAAGCAGATCAGG  
AAAAGTGTTGGGGTTTTGACCAGTTTTTTGCAGAACTAGTGATATACTTCACCGAATGG  
TAATTCATGTTTTTTCGCTACAACAATGACAGCTCATAAGATTTATATTATAGCTATA  
ATACTGCTACTATATTTTATGAAGTGGTATATAAACAACCAAATTTATTTCTTCAAATC  
AAGAACTTATCTACGAAGGGCGACGCTTAGTCTTAGAACCTGGAAGGCTGGCACAACAT  
TCCCTAAACTACTGAGGAAAACCTTATATTTGTAGTAAGCCGGGAACCTCTGAATACCA  
TAGGATTAATATATGAAAAAATTTCCCTCCCTAAAGTACATCCACGTTATGATTTAGACG  
GGGATGCTAGCATGGCTAAGGCAATAACAGGGGTGTGTGTTATGCCTGCAGAATTGCCA  
GTACCTTACTGCTTTATCAGGAATTAATGCGAAAGGGGATACGATGGCTGATTGAATTAA  
TTAAAGATGATTACAATGAACTGTTCAAAAAAGACAGAAGTTGTGATCACATTGGATT  
TCTGTATCAGAAACATTGAAAAAACTGTGAAAGTATATGAAAAGTTGATGAAGATCAACC  
TGGAAGCGGCAGAGTTAGGTGAAATTTTCAGACATACACACCAAATTTGTTGAGACTTTCCA  
GTTCTCAGGGAACAATAGAAACCACTTTCAGGATATCGACAGCAGATTATCTCCAGGTG  
GATCACTGGCAGACGCATGGGCACATCAAGAAGGCACTCATCCGAAAGACAGAAATGTAG  
AAAACTACAAGTCTGTAAATTCATGACAGAGATTTACTATCAGTTCAAAAAAGACA  
AAGCAGAACGTAGATTAGCTTATAATGAAGAACAATCCACAAATTTGATAAGCAAAAAAC  
TGTATTACCATGCCACAAAAGCTATGACGCACTTTACAGATGAATGTGTTAAAAAGTATG  
AGGCATTTTTGAATAAGTCAGAAGAATGGATAAGAAAGATGCTTCATCTTAGGAAACAGT  
TATTATCGCTGACTAATCAGTGTTTTGATATTGAAGAAGAAGTATCAAAATATCAAGAAT  
ATACTAATGAGTTACAAGAACTCTGCCTCAGAAAATGTTTACAGCTTCCAGTGGAATCA  
AACATAACCATGACCCCAATTTATCCAAGTTCTAACACATTAGTAGAAATGACTCTTGGA  
TGAAGAAATTAAGGAAGAGATGGAAGGGGTGGTTAAAGAACTTGCTGAAAATAACCACA  
TTTTAGAAAGGTTTGGCTCTTTAACCATGGATGGTGGCCTTCGCAACGTTGACTGTCTTT  
AGCTTTCTAATAGAAGTTTAAGAAAAGTTTCCGTTTGACAAGAAAATAACGCTTGGGCA  
TTAAATGAATGCCTTTATAGATAGTCACTTGTCTTACAATCCAGTATTTGATGTGGTCCG  
TGTAATATGTACAATATTGTAAATACATAAAAAATATACAAATTTTGGCTGCTGTGAA  
GATGTAATTTTATCTTTTAACATTTATAATTATATGAGGAAATTTGACCTCAGTGATCAC  
GAGAAGAAAGCCATGACCGACCAATATGTTGACATACTGATCCTCTACTCTGAGTGGGGC  
TAAATAAGTTATTTTCTCTGACCGCCTACTGGAAATATTTTAAAGTGAACCAAATAGG  
CATCCTTACAATCAGGAAGACTGACTTGACACGTTTGTAAATGGTAGAACGGTGGCTAC  
TGTGAGTGGGGAGCAGAACCGCACCCTGTTATACTGGGATAACAATTTTTTGAAGG  
ATAAAGTGGCATTATTTTATTTTACAAGGTGCCAGATCCAGTTATCCTTGTATCCATG  
TAATTTAGATGAATTATTAAGCAAACATTTTAAAGTGAATTCATTATTAAGAACTATTC  
ATTTTTTCTTTGGCCATAAATGTGTAATTGTCATTAAATTTCTAAGGTCATTTCAACT

## FIGURE 2E

GTTTTAAGCTGTATATTTCTTTAATTCTGCTTACTATTTTCATGGAAAAAATAAATTTCT  
CAATTTTAAAAAA

SEQ ID NO: 6\_AA305176\_H

TGGCTGCTCGCGGAGGGGCAGTGTACGCGGGGCCGCTGTAGGCTGTCCAGCGATGGATCC  
CACCGCGGGAAGCAAGAAGGAGCCTGGAGGAGGCGCGGCGACTGAGGAGGGCGTGAATAG  
GATCGCAGTGCCAAAACCGCCCTCCATTGAGGAATTCAGCATAGTGAAGCCCATTAGCCG  
GGGCGCCTTCGGGAAAGTGTATCTGGGGCAGAAAGGCGGCAAATTGTATGCAGTAAAGGT  
TGTTAAAAAAGCAGACATGATCAACAAAAATATGACTCATCAGGTCCAAGCTGAGAGAGA  
TGCCTGGCACTAAGCAAAAGCCCATTTCATTGTCCATTTGTATTATTCACTGCAGTCTGC  
AAACAATGTCTACTTTGTAATGGAATATCTTATTGGGGGAGATGTCAAGTCTCTCCTACA  
TATATATGGTTATTTTGATGAAGAGATGGCTGTGAAATATATTTCTGAAGTAGCACTGGC  
TCTAGACTACCTTCACAGACATGGAATCATCCACAGGGACTTGAAACCGGACAATATGCT  
TATTTCTAATGAGGGTCATATTAACTGACGGATTTTGGCCTTTCAAAGTTACTTTGAA  
TAGAGATATTAATATGATGGATATCCTTACAACACCATCAATGGCAAAACCTAGACAAGA  
TTATTCAAGAACCCCAGGACAAGTGTTATCGCTTATCAGCTCGTTGGGATTTAACACACC  
AATTGCAGAAAAAATCAAGACCTGCAAAACATCCTTTAGCCTGTCTGTCTGAAACATC  
ACAGCTTTCTCAAGGACTCGTATGCCCTATGTCTGTAGATCAAAGGACACTACGCCTTA  
TTCTAGCAAATTACTAAAATCATGTCTTGAAACAGTTGCCTCCAACCCAGGAATGCCTGT  
GAAGTGTCTAATTCTAATTTACTCCAGTCTAGGAAAAGGCTGGCCACATCCAGTGCCAG  
TAGTCAATCCCACACCTTCATATCCAGTGTGGAATCAGAATGCCACAGCAGTCCCAAATG  
GGAAAAAGATTGCCAGGTTTGAGGGACATTTATCTTAATGAAAATCAATTATGTATGTCA  
AATGAATGTGAGAAATATTATACCTTTTTCATATAAATTCCATAAAGAAATGAAATTGTTA  
CATGAATGGCAGTCATAGTATTAATCAGAAATTCATTTTCTGCACATTCTGTCAAATTC  
TTTTGAAATATTTTCATTTCTCATTCAATTGTGACATTGTTCTTACTTGATTATATAATGA  
GATTCTTGCAGTAAATTGATAATAAATGCTTGGCTTCTGTGTATCTAGGTGGACCTCACT  
TGTTTTTAGAAGTCCTTCCCATGATACAGACATTGGCTTGTGGTTTTGTTTTATTTTGT  
TTTTAACATATGTCAATTTAAAACTCATATTACCTCCTTTT

SEQ ID NO: 7\_AA116841\_M

CCACGCGTCCGATCCCATGGCCAGAAGGCGAAGAAAAGCTATCTGATAATGCTCAAAGTG  
CAATGGACATGCTTTTAACCATTGATGATTCAAAGAGAGCTGGAATGAGAGAACTAAAC  
AGCATCCTCTCTTCAGTGAAGTGGACTGGGAAAATCTGCAGCATCAGACTATGCCTTTTCG  
TACCCCAACCAGACGACGAAACAGATACATCCTATTTTGAAGCCAGAAATAATGCTCAAC  
ATCTGACCGTATCTGGGTTTAGTCTGTAGCACATGCGTGTCAATTTTTATCTAATTGTGA  
TATAGAATTAAGTTTTACAGTAATATGCTACTTAATACTAGATTGGTCTAAATGGGATAA  
AAGTCATTATTTTACCCAGACTGAACAGCTTTTAATTACTAAGTACAACAGTTTTTACAG  
AATTAAAATACTATAAGCAATATAATCAGTAATTAATCTTTACCTTAGAAGTGTATATAA  
GCCATAATAGCTTTTTTTCATCTTATTTATTCAGTCACTTTATGAAGAGCAAAGTATCAA  
TAACTAAAACACTACCACTCTAAATAGAGGGAGTGAGCCGT

SEQ ID NO: 8\_AA256100\_H

AGGGAGCTGACGGGCGCCGGCGGCTGCGGTCCGTGCGGAGGCTGAGCCGGCGCGGGC  
GCGACCGGAGGCAGTTTCCGTTACTATGGCAATGACGGCAGGGACTACAACAACCTTTCC  
TATGAGCAACCATAACCCGGGAAAGAGTGACTGTAGCCAAGCTCACATTGGAGAATTTTAA  
TAGCAACCTAATTTTACAGCATGAAGAGAGAGAAACCAGGCAGAGAAATTAGAAGTGCC  
CATGGAAGAAGAAGGATTAGCAGATGAAGAGAAAAAGTTACGTCGATCACAAACACGCTCG  
CAAAGAAACAGAGTTCTTACGGCTCAAAAGGACCAGACTTGGCTTGGATGACTTTGAGTC  
TCTGAAAGTTATAGGAAGAGGAGCTTTTGGAGAGGTGCGGTTGGTCCAGAAGAAAGATAC  
AGGCCATATCTATGCAATGAAGATATTGAGAAAGTCTGATATGCTTGAAAAAGAGCAGGT



## FIGURE 2F

GGCCCATATCCGAGCAGAAAGAGATATTTTGGTAGAAGCAGATGGTGCCTGGGTGGTGAA  
GATGTTTTACAGTTTTTCAGGATAAGAGGAATCTTTATCTAATCATGGAATTTCTCCCTGG  
AGGTGACATGATGACATTGCTAATGAAGAAAGACACCTTGACAGAAGAGGAAACACAGTT  
CTACATTTTCAGAGACTGTTCTGGCAATAGATGCGATCCACCAGTTGGGTTTCATCCATCG  
GGATATTAAGCCAGACAACCTTTTATTGGATGCCAAGGGTCATGTAAAATTATCTGATTT  
TGGTTTATGTACGGGATTAAAGAAAGCTCACAGGACTGAATTTTATAGAAATCTCACACA  
CAACCCACCAAGTGACTTCTCATTTTCAGAACATGAACTCAAAGAGGAAAGCAGAACTTG  
GAAGAAGAACAGGAGACAACCTGGCATATTCCACAGTTGGGACACCAGATTACATTGCTCC  
AGAAGTATTCATGCAGACTGGTTACAACAAATTGTGTGACTGGTGGTCTTTGGGAGTGAT  
TATGTATGAAATGCTAATAGGATATCCACCTTTCTGCTCTGAAACACCTCAAGAAACATA  
CAGAAAAGTGATGAACTGGAAAGAACTCTGGTATTTCTCCAGAGGTACCTATATCTGA  
GAAAGCCAAGGACTTAATTCTCAGATTTTGTATTGATTCTGAAAACAGAATTGGAAATAG  
TGGAGTAGAAGAAATAAAGGTCATCCCTTTTTTGAAGGTGTGACTGGGAGCACATAAG  
GGAAAGGCCAGCAGCAATCCCTATAGAAATCAAAGCATTGATGATACTTCAAATTTTGA  
TGACTTCCCTGAATCTGATATTTTACAACCAGTGCCAAATACCACAGAACCGGACTACAA  
ATCCAAAGACTGGGTTTTTCTCAATTATACCTATAAAAGGTTTGAAGGGTTGACTCAACG  
TGGCTCTATCCCCACCTACATGAAAGCTGGGAAGTTATGAATGAAGATAACATTCACCCA  
TAACCAAGAGAACTCAGGTAGCTGCATCACCAGGCTTGCTTGGCGTAGATAACAATACAC  
TGAAATACTCCTGAAGATGGTGGTGCTTATTGACTACAAGAGGAAATTCTACAGGATTAG  
GATTTCTAAGACTACTATAGGAATTGGTTGGCAGTGCCAGCTGGCTCTTTTTTTTAAATAT  
TTTATTATTTTTTGTAACTTTATTATATGAAGGTACTGGAATAAAAGGAACAGACATCCC  
TTTCTAACTGCACTGCCTACATGCGTATTAAGGTCCATTCTGCCTGTGTGTGCTGTGGCT  
TTGAACTGTAAACACCTCTAATCAATTCAGGAGAAACACATATCATTTAAAGCAACATAGG  
CTAACCTGTAGGTAACTGCAGTATTGATGTTTTTACTGCAAATCTTATGGGTCTAGATA  
ATCAGTAAAAGCCATCTTCCATAGTTGGTGTTAGAACATTGCCCTATTGGTTTGGACATC  
TGTAGAATATATATGAAGACAATTTCTGTAATGGTTTTAAGAGATTTAAAAGAAATTCA  
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TGACAAGTTTATAATAAGGAAGACAAAGTTTAAACACCTTCACTCAAGCACTCCACTAATA  
TATTTACGTTGCATTCAGAAATACTGATGACCTTCATATACGTAGTCTGTATACTCATAG  
GGAGATGTACTGTATTATATAACATGTAAAGTTGATTTTCTTGTGACAAGAGAACTTCTT  
TTTTTAAACAAGAGGACATGGCATTATTTTAAATTTGATTATGGTGAGTTGAATTTAAGACA  
TGACCATGAAGGCTGCTTGTAGAATTAGTGTATTTTATTAACTATTTTTTTTAAATGTC  
AACTTCTATCATGTAAATGGACTTATAGAGAACAAAAGCTATTTACTTTGGTTTTCTA  
GAAAGTTGTTACATATCATGGCTGGTTAACTTTTATTTCTTTTGATGAAAATTTTCTCTT  
TGATAGTACTTGTATTATTGTGCCATTATTTTCTTATGCTCCAAATGTACCAAAGATCTT  
GAACAGAGTGATGTTTCACTGAGTAGAATTTTCTTTCTGTGGGCATGCTGTATTCT  
AGACCTGACAGATCTTTGATAGAGGTCAGCTTATTAAGGGCAATATTGTTCTTGTGTTAG  
CTACATCACTGTGGTGAATATAGATGGAATTAAGGAAGTAAATGCAGGCCAGGGGGTTGT  
GATGAGAGGATAGGGGAGATAATATCAGCATCAAATTCTTTGGGTATCTCTCTAAGAATT  
AAATAATCTTTTCTAGCTTAATATTTTAAATTCTAATTCAAACAACCTCTGAGGTTTTGGTT  
TCATTAGTAATAGTTGAGGAATAATACTAGCAAAGAATGGCCTAATGTTTGTCTATAAC  
TGTTAATGGATGAAATTTTTTAAAGATACAACCATGATAACCATTATAAATGATCTATGA  
TCAAATCTAAAGTGATGAATTATTTGTAGGAATGTCTTCTAATGGGGAAGAATTGCAT  
AGGAGCATTATGCAAATCTACACAAGCTTTTATAAATGTTGCTGCTGGGTAGCTCCACAG  
TGTTTCATAAGGCCATCCTGTTTCCCCCACTCCCCATTTTTGGTTTGTCTTTTTTAA  
ATATTTGTTGAGTACTTACGTGTTTATCTAACAGTTCACTTCCATTTTTCTAGTCTGGAT  
TTTTTGGATATTTAGGAAAGAGAGCTATTAAAAACCTCTGGGATTTCTCAATGTGACTAA  
CTCTAATTTTTCTAATTATACTGCCTTTAATTAACATAATTAACTTTTGCTGAGGTT  
TATGAGATTTTCTCACCCACATCGCTCCCTTTTTTTAAAAGGACTGTTTTGCTAGTG  
TGATAATGAATAGGTAAGATATGAGATAATTGCAACATTGTCCTAGTCTAGTATGGTAA



## FIGURE 2G

CTATTCTTGAAATGGTATTGAAAAATACCGTTAATTCAAATTGACAGAGATTGATAAAAA  
GAACTGATTTACCTAAGTTTACTTTTTTAATTGCATAATAGAGCATTTTTTGTGTTT  
TCCCTCATTCTTATTACCAGAAAGAGCTTGCAAATAGTTTTACTTTCTTGGCACTGGAAG  
GGTAGTCTGGAAAGCTACTTTGTTGAGAGTCTCATTCTTCCCTGGAGTTAATAGAGTGA  
TTCACAATCTTTGGGGTTTTCTCCTCATCAAAGCATTCTTAAGTGCCTATCTAAAAGC  
AATTAAAGACTGTGTCTGCCCTTTAGAAGCTAAGAATTTGATTCATGATGCAAATTAAC  
AGATAATTTGCAAAGTACCTTGAGATTGAATTTTCTCTATTATATATTTCCCATATTT  
AGGTGAATAATTTAATTTAAATGACAAAACCTATCTAGTCAACTGGGCATAATGACATT  
TTCTTTAAATTAGACTCTATTTTGAATTAAAAGAGTTTTATTATAAACCGTGTGTTTTG  
GTTTTCTAAGTATATAGAAAGCTTGTATAATTCAGATTTATCAATTTCTGATTTAATG  
TAGACTTTGACTTTTTTTATTA AAAACCTTTGTATTAAAGCAAGTTATGTTATTTTTCTTT  
TATGCATTTATTACTAACATAGCTTTAAATCTTTAAATGTATTGAAGCATTGTGCTGTCT  
GAAAATAAGGAATTGCTTATAAACAGCCACTTCTGAATACAATATGTAGCTGATTTAAT  
AAGCTAGTTAGTGAATGGAAAATAAGTGTGGAGTATTA AAAATGTTCTTTGGTTGGTAAG  
GCCTAAGATAGGGTTTCATTTATTTCTATACTTTTTCTGTTTTTTAAACACCTGCATATT  
TTTATGTAAATCTCTAAATTTAAATATTTTTAAGTACATTTATTTTTGGTGTGTTTATTGT  
ATAAACCTTAGACAATCAATCAGTCAGTCTTTACTGACAGGAGCAGCAGCTATCTGTCT  
TTTGCTGATCTACAAATAAATGAATTGAGAATTTAGTCCATAGAGGTCCCTGGCTACCAA  
ACACATTCTCCTTTGAATTGTTAAAATTCAGAACATTCAAAAATACTGTTTTGCTACAAC  
CCATGATTATTTTCTGTTGTGTTTATTTAAATTTACTTTCTCTTTAGAAGTGCATTTAT  
TTCTGAAAAATCTTAATGAAACAAACGCTTAGAACAAATATAAATATGAGACACTTGGGA  
CTACTAGAGATATTTTAGATTTTTATGAAAAAATGTGAGGGGATATTGCTGCTTTAAAA  
AGGAATAAAGTAATAAAAATATATCTCAGCTATTTTTTTAAAGCAATATAATTCAGCAAT  
TGTCTAGAAAAGTAATCATGAGGCTACTGAGTTTGGTGTTCAGTTACTGAGTTTCAAAA  
TGTTTTGGTGGCATGAGGACAAAATTTCAATTGAAGGTAAGATAAGAATAAAAACCTATGTT  
TAC

SEQ ID NO: 9\_AA210825\_H

CACGAGGGCTACTGGCGCCTGGCGACCCTCCCTGCCCCCACCCAACCCGCTCCGGCAA  
CGCCCCCTTCCCTCACGGCTCCCGACCGAACTTTTCTCCAACCTCTGCGACTCGTGAGATT  
CCCTTCTACCCACTCCGGCCCTCGGGACCCCTCTGCCCATCCCTGGCCGGTCCGGTCCC  
TGCGAACCCCTTTATCTCTGGAATCCACTCGGTCCCCGACTCAGAGACTCCTGCCCTCCA  
CCCCCAAGGACCCCGCCATCCTCAGGTCCCCCTCCGCTGCCAGATCTTTTCTCGGATCCC  
CGCTCTCCCAACCTGCTCACGAGATCCCGCGGATCTAGAACCAGGGTCCCCCGGGC  
CCCCCGGCGGGTCCCGGGTGGGCTCCAGGCGGGCGGTCCCCGGCCTCCCCCATGGCCAC  
CGCCCCCTCATTATCCCGCCGGGCTCCCTGGCTCTCCCGGGCCGGGGTCTCCTCCGCCCC  
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CCGGGGTCTCCTTTACATCCAGATCGGGCTGACCCGCGAGTTTCGTGCTGTTGCCCGCCG  
CCTCCGAGCTGGCTCATGTGAAGCAGCTGGCCTGTTCCATCGTGGACCAGAAGTTCCCTG  
AGTGTGGCTTCTACGGCCTTTACGACAAGATCCTGCTTTTCAAACATGACCCACGTCCG  
CCAACCTCCTGCAGCTGGTGCCTCGTCCGGAGACATCCAGGAGGGCGACCTGGTGGAGG  
TGGTGTGTGGCCTCGGCCACCTTCGAGGACTTCAGATCCGCCCGCACGCCCTCACGG  
TGCACTCCTATCGGGCGCCTGCCTTCTGTGATCACTGCGGGGAGATGCTCTTCGGCCTAG  
TGCGCCAGGGCCTCAAGTGCGATGGCTGCGGGCTGAACCTACCACAAGCGCTGTGCCTTCA  
GCATCCCCAACAACTGTAGTGGGGCCCGCAAACGGCGCCTGTATCCACGTCTCTGGCCA  
GTGGCCACTCGGTGCGCCTCGGCACCTCCGAGTCCCTGCCCTGCACGGCTGAAGAGCTGA  
GCCGTAGCACCACTGAACCTCGCCTCGCCGTCCCCCGTCATCCTCTTCTCTCTCTCTG  
CCTCATCGTATACGGGCCGCCCATTTGAGCTGGACAAGATGCTGCTCTCCAAGGTCAAGG  
TGCCGCACACCTTCTCATCCACAGCTATACACGGCCACCGTTTGCCAGGCTTGCAAGA  
AACTCCTCAAGGCCTCTTCCGGCAGGGCCTGCAATGCAAAGACTGCAAGTTTAACTGTC

## FIGURE 2H

ACAAACGCTGCGCCACCCGCGTCCCTAATGACTGCCTGGGGGAGGCCCTTATCAATGGAG  
ATGTGCCGATGGAGGAGGCCACCGATTTTCAGCGAGGCTGACAAGAGCGCCCTCATGGATG  
AGTCAGAGGACTCCGGTGTTCATCCCTGGCTCCCACTCAGAGAATGCGCTCCACGCCAGTG  
AGGAGGAGGAAGGCGAGGGAGGCAAGGCCAGAGCTCCCTGGGGTACATCCCCCTAATGA  
GGGTGGTGCAATCGGTGCGACACACGACGCGGAAATCCAGCACCACGCTGCGGGAGGGTT  
GGGTGGTTTATTACAGCAACAAGGACACGCTGAGAAAGCGGCACTATTGGCGCCTGGACT  
GCAAGTGTATCACGCTCTTCCAGAAACAACGACCAACAGATACTATAAGGAAATTCGCG  
TGTCAGAAATCCTCACGGTGGAGTCCGCCCAAGAACTTCAGCCTTGTGCCGCCGGGCACCA  
ACCCACACTGCTTTGAGATCGTCACTGCCAATGCCACCTACTTCGTGGGCGAGATGCCTG  
GCGGGACTCCGGGTGGGCCAAGTGGGCAGGGGGCTGAGGCCGCCCGGGGGCTGGNNGAGA  
CAGCCATCCGCCAGGCCCTGATGCCCCGTATCCTTCAGGACGCACCCAGCGCCCCAGGCC  
ACGCGCCCCACAGACAAGCTTCTCTGAGCATCTCTGTGTCCAACAGTCAGATCCAAGAGA  
ATGTGGACATTGCCACTGTCTACCAGATCTTCCCTGACGAAGTGCTGGGCTCAGGGCAGT  
TTGGAGTGGTCTATGGAGGAAAACACCGGAAGACAGGCCGGGACGTGGCAGTTAAGGTCA  
TTGACAACTGCGCTTCCCTACCAAGCAGGAGAGCCAGCTCCGGAATGAAGTGGCCATTC  
TGCAGAGCCTGCGGCATCCCGGGATCGTGAACCTGGAGTGCATGTTTCGAGACGCCTGAGA  
AAGTGTGTGTGGTGATGGAGAAGCTGCATGGGGACATGTTGGAGATGATCCTGTCCAGTG  
AGAAGGGCCGGCTGCCTGAGCGCCTCACCAAGTTCTCTCATCACCAGATCCTGGTGGCTT  
TGAGACACCTTCACTTCAAGAACATTGTCCACTGTGACTTGAAACCAGAAAACGTGTTGC  
TGGCATCAGCAGACCCATTTCTCTCAGGTGAAGCTGTGTGACTTTGGCTTTGCTCGCATCA  
TCGGCGAGAAGTTCGTTCCGCCGCTCAGTGGTGGGCACGCCGGCCTACCTGGCACCCGAGG  
TGCTGCTCAACCAGGGCTACAACCGCTCGCTGGACATGTGGTCAGTGGGCGTGATCATGT  
ACGTGACCTCAGCGGCACCTTCCCTTTCAACGAGGATGAGGACATCAATGACCAGATCC  
AGAACGCCGCCCTTCATGTACCCGGCCAGCCCCCTGGAGCCACATCTCAGCTGGAGCCATTG  
ACCTCATCAACAACCTGCTGCAGGTGAAGATGCGCAAACGCTACAGCGTGGACAAATCTC  
TCAGCCACCCCTGGTTACAGGAGTACCAGACGTGGCTGGACCTCCGAGAGCTGGAGGGGA  
AGATGGGAGAGCGATACATCACGCATGAGAGTGACGACGCGCGCTGGGAGCAGTTTGCAG  
CAGAGCATCCGCTGCCTGGGTCTGGGCTGCCACGGACAGGGATCTCGGTGGGGCCTGTG  
CACCACAGGACCACGACATGCAGGGGCTGGCGGAGCGCATCAGTGTCTCTGAGGTCTG  
TGCCCTCGTCCAGCTGCTGCCCTCCACAGCGGTTCTTACAGGATCCCAGCAATGAAGT  
TTCTAGGGAAAGTGGCTTCTTGCCCAAACCTGGATGGGACACGTGGGGAGTGGGGTGGGG  
GAGCTATTTCCAAGGCCCTCCCTGTTTCCCCAGCAATTAACGAGTCTATCTCTGGCC  
CCATGGCCTTGATCTCAGCAAAA

SEQ ID NO: 10\_AA127299\_H

ATTCAATTCATAATTGTTGGTGCAAAAGATTTGCTTGCTATGGATTCAAATGGTCTTTCT  
GATCCTTACATCAAAATCACAATCTTTCTCAAAAAACGAAAGTGATTAAGAAAACCTTG  
ACTCCAACCTTGAATGAAACTTTTTTTGTGCATTTTCCAGAAAAACAACCTTGAATTA  
GAATGTTGGGACCACGATACTTTTTCAGATGATTTTATTGGCAAGGCTTCCATTTCTTTG  
GCAGAGATTCCAGCTTTGGCAGAAGTTGATATGTGGATAGATATGAAAACGAAAAAAGGA  
GAATTTGCAGGAAAA

SEQ ID NO: 11\_AA316804\_H

ATGTCTGCAAATAATTCCCCTCCATCAGCCCAGAAGTCTGTATTACCCACAGCTATTCCCT  
GCTGTGCTTCCAGCTGCTTCTCCGTGTTCAAGTCCTAAGACGGGACTCTCTGCCCCGACTC  
TCTAATGGAAGCTTTCAGTGCACCATCACTACCAACTCCAGAGGCTCAGTGCATACAGTT  
TCATTTCTACTGCAAATTGGCCTCACACGGGAGAGTGTTACCATTGAAGCCCAGGAACTG  
TCTTTATCTGCTGTCAAGGATCTTGTGTGCTCCATAGTTTATCAAAAGTTTCCAGAGTGT  
GGATTCTTTGGCATGTATGACAAAATCTTCTCTTTCCGCCATGACATGAACTCAGAAAAC  
ATTTTGCAGCTGATTACCTCAGCAGATGAAATACATGAAGGAGACCTAGTGAAGTGGTT

FIGURE 21

CTTTCAGCTTTAGCCACAGTAGAAGACTTCCAGATTTCGTCCACATACTCTCTATGTACAT  
TCTTACAAAGCTCCTACTTTCTGTGATTACTGTGGTGAGATGCTGTGGGGATTGGTACGT  
CAAGGACTGAAATGTGAAGGCTGTGGATTAAATTACCATAAACGATGTGCCTTCAAGATT  
CCAAATAACTGTAGTGGAGTAAGAAAGAGACGTCTGTCAAATGTATCTTTACCAGGACCC  
GGCCTCTCAGTTCCAAGACCCCTACAGCCTGAATATGTAGCCCTTCCCAGTGAAGAGTCA  
CATGTCCACCAGGAACCAAGTAAGAGAATTCCTTCTTGGAGTGGTCGCCCCAATCTGGATG  
GAAAAGATGGTAATGTGCAGAGTGAAAGTTCCACACACATTTGCTGTTCACTCTTACACC  
CGTCCCACGATATGTCACTACTGCAAGCGGTTACTGAAAGGCCTCTTTCGCCAAGGAATG  
CAGTGTAAGATTGCAAATTCAACTGCCATAAACGCTGTGCATCAAAAGTACCAAGAGAC  
TGCCTTGGAGAGGTTACTTTCAATGGAGAACCTTCCAGTCTGGGAACAGATACAGATATA  
CCAATGGATATTGACAATAATGACATAAATAGTGATAGTAGTCGGGGTTTGGATGACACA  
GAAGAGCCATCACCCCAGAAGATAAGATGTTCTTCTTGGATCCATCTGATCTCGATGTG  
GAAAGAGATGAAGAAGCCGTTAAAACAATCAGTCCATCAACAAGCAATAATATTCCGCTA  
ATGAGGGTTGTACAATCCATCAAGCACACAAAGAGGAAGAGCAGCACAATGGTGAAGGAA  
GGGTGGATGGTCCATTACACCAGCAGGGATAACCTGAGAAAGAGGCATTATTGGAGACTT  
GACAGCAAATGTCTAACATTATTTTCAAGATGAATCTGGATCAAAGTATTATAAGGAAATT  
CCACTTTCAGAAATTCCTCCGCATATCTTACCACGAGATTTTCAAAACATTTTACAAGGC  
AGCAATCCACACTGTTTTGAAATCATTACTGATACTATGGTATACTTTCGTTGGTGAGAAC  
AATGGGGACAGCTCTCATAATCCTGTTCTTGTGCTGCCACTGGAGTTGGACTTGATGTAGCA  
CAGAGCTGGGAAAAAGCAATTCGCCAAGCCCTCATGCCTGTTACTCCTCAAGCAAGTGTT  
TGCACCTTCTCCAGGGCAAGGGAAAGATCACAAGATTTGTCTACAAGTATCTCTGTATCT  
AATTGTGAGATTCAGGAGAATGTGGATATCAGTACTGTTTACCAGATCTTTCAGATGAG  
GTGCTTGGTTTCAGGCCAGTTTGGCATCGTTTATGGAGGAAAACATAGAAAGACTGGGAGG  
GATGTGGCTATTAAAGTAATTGATAAGATGAGATTCCTCCACAAAACAAGAAAGTCAACTC  
CGTAATGAAGTGGCTATTTTACAGAATTTGCACCATCCTGGGATTGTAAACCTGGAATGT  
ATGTTTGAAACCCCAAGACGAGTCTTTGTAGTAATGGAAAAGCTGCATGGAGATATGTTG  
GAAATGATTCTATCCAGTGAGAAAAGTCGGCTTCCAGAACGAATTACTAAATTCATGGTC  
ACACAGATACTTGTGCTTTGAGGAATCTGCATTTTAAAGAATATTGTGCACTGTGATTTA  
AAGCCAGAAAATGTGCTGCTTGCATCAGCAGAGCCATTTCTCAGGTGAAGCTGTGTGAC  
TTTGGATTTGCACGCATCATTGGTGAAAAGTCATTTCAGGAGATCTGTGGTAGGAACCTCA  
GCATACTTAGCCCCGAAGTTCTCCGGAGCAAAGGTTACAACCGTTCCCTAGATATGTGG  
TCAGTGGGAGTTATCATCTATGTGAGCCTCAGTGGCACATTTCTTTTAAATGAGGATGAA  
GATATAAATGACCAAATCCAAAATGCTGCATTTATGTACCCACCAAATCCATGGAGAGAA  
ATTTCTGGTGAAGCAATTGATCTGATAACAATCTGCTTCAAGTGAAGATGAGAAAACGT  
TACAGTGTTGACAAATCTCTTAGTCATCCCTGGCTACAGGACTATCAGACTTGGCTTGAC  
CTTAGAGAATTTGAAACTCGCATTGGAGAACGTTACATTACACATGAAAGTGATGATGCT  
CGCTGGGAAATACATGCATACACATAACCTTGTATACCCAAAGCACTTCATTATGGCT  
CCTAATCCAGATGATATGGAAGAAGATCCTTAA

SEQ ID NO: 12\_PKNBETA\_H

ATGGAGGAGGGGGCGCCGCGGCAGCCTGGGCGGAGCCAGTGGCCCCCAGAGGATGAGAAG  
GAGGTGATCCGCGGGGCCATCCAGAAAGAGCTGAAGATCAAGGAGGGGGTGGAGAACCTG  
CGGCGCGTGGCCACAGACCGCCGCACTTGGGCCATGTGCAGCAGCTGCTGCGGTCTCC  
AACCGCCGCTGGAGCAGCTGCATGGCGAGCTGCGGGAGCTGCACGCCCCGAATCCTGCTG  
CCCCGGCCCTGGGCCTGGCCCAGCTGAGCCTGTGGCCTCAGGACCCCGGCGCTGGGCAGAG  
CAGCTCAGGGCTCGGCACCTAGAGGCTCTCCGGAGGCAGCTGCATGTGGAGCTGAAGGTG  
AAACAGGGGGCTGAGAACATGACCCACACGTGCGCCAGTGGCACCCCCAAGGAGAGGAAG  
CTCCTTGACAGCTGCCACAGCAGATGCTGCGGGACAGCCAGCTGAAGGTGGCCCTGCTGCGG  
ATGAAGATCAGCAGCCTGGAGGCCAGTGGGTCCCCGGAGCCAGGGCCTGAGCTACTGGCG  
GAGGAGCTACAGCATCGACTGCACGTTGAGGCAGCGGTGGCTGAGGGCGCCAAGAACGTG

FIGURE 2J

GTGAAACTGCTTAGTAGCCGAGAACACAGGACCGCAAGGCACTGGCTGAGGCCAGGCC  
CAGCTACAGGAGTCCTCTCAGAACTGGACCTCCTGCGCCTGGCCTTGGAGCAGCTGCTG  
GAGCAACTGCCTCCTGCCCACCCCTTTGCGCAGCAGAGTGACCCGAGAGTTGCGGGCTGCG  
GTGCCTGGATACCCCCAGCCTTCAGGGACACCTGTGAAGCCCCACCGCCCTAACAGGGACA  
CTGCAGGTCCGCCTCCTGGGCTGTGAACAGTTGCTGACAGCCGTGCCTGGGCGCTCCCCA  
GCGGCCGCACTGGCCAGCAGCCCCCTCCGAGGGCTGGCTTCGGACCAAGGCCAAGCACCAG  
CGTGGCCGAGGCGAGCTTGCCAGTGAGGTGCTGGCTGTGCTAAAGGTGGACAACCGTGTT  
GTGGGGCAGACGGGCTGGGGGCAGGTGGCCGAACAGTCCTGGGACCAGACCTTTGTCTC  
CCACTGGAGCGAGCCCGTGAGCTGGAGATTGGGGTACACTGGCGGGACTGGCGGCAGCTA  
TGTGGCGTGGCCTTCCCTGAGACTTGAAGACTTCCTGGACAATGCCTGTCACCAACTGTCC  
CTCAGCCTGGTACCGCAGGGACTGCTTTTTGCCAGGTGACCTTCTGCGATCCTGTCTATT  
GAGAGGCGGCCCGGCTGCAGAGGCAGGAACGCATCTTCTCTAAACGCAGAGGCCAGGAC  
TTCCTGAGGCGTTTCGAGATGAACCTCGGCATGGCGGCCTGGGGGCGCCTCGTCATGAAC  
CTGCTGCCCCCCTGCAGCTCCCCGAGCACAATCAGCCCCCCTAAAGGATGCCCTCGGACC  
CCAACAACACTGCGAGAGGCCTCTGACCCTGCCACTCCAGTAATTTCTGCCCCAAGAAG  
ACCCCTTGGGTGAAGAGATGACACCCCCACCAAGCCCCACGCCTCTACCTCCCCAG  
GAGCCAACATCCGAGGAGACTCCGCGCACCAACGTCCCCATATGGAGCCTAGGACTCGA  
CGTGGGCCATCTCCACCAGCCTCCCCACCAGGAAACCCCTCGGCTTCAGGACTTCCGC  
TGCTTAGCTGTGCTGGGCGGGGACACTTTGGGAAGGTCTCCTGGTCCAGTTCAAGGGG  
ACAGGGAAATACTACGCCATCAAAGCACTGAAGAAGCAGGAGGTGCTCAGCCGGGACGAG  
ATAGAGAGCCTGTACTGCGAGAAGCGGATCCTGGAGGCTGTGGGCTGCACAGGGCACCCT  
TTCCTGCTCTCCCTCCTTGTCTGCTTCCAGACCTCCAGCCATGCCCGCTTTGTGACTGAG  
TTTGTGCCTGGTGGTGACCTCATGATGCAGATCCACGAGGATGTCTTCCCCGAGCCCCAG  
GCCCCGTTCTACGTGGCTTGTGTTGTCTGGGGCTGCAGTTCTTACACGAGAAGAAGATC  
ATTTACAGGGACCTGAAGTTGGATAACCTTCTGCTGGATGCCAGGGATTCTTGAAGATC  
GCAGACTTTGGACTCTGCAAGGAAGGGATCGGCTTCGGGGACCGGACTAGCACCTTCTGT  
GGCACCCCGGAGTTCTGGCTCCCGAGGTGCTGACCCAGGAGGCATACACAGGCCGTC  
GACTGGTGGGCGCTGGGTGTGCTGCTCTACGAGATGCTGGTGGGTGAGTGCCCGTTCCCA  
GGGGACACAGAGGAAGAGGTGTTTACTGCATCGTCAACATGGACGCCCCCTACCCCGGC  
TTTCTGTGCGTGCAAGGGCTTGAGTTCATTGAGAAGCTCCTCCAGAAGTGCCCGGAGAAG  
CGCCTCGGGGCAGGTGAGCAGGATGCCGAGGAGATCAAGGTCCAGCCATTCTTCAGGACC  
ACCAACTGGCAAGCCCTGCTCGCCCGCACCATCCAGCCCCCTTCGTGCCTACCCTGTGT  
GGCCCTGCGGACCTGCGCTACTTTGAGGGCGAGTTCACAGGGCTGCCGCTGCCCTGACC  
CCACCTGCACCCACAGCCTCCTCACTGCCCGCCAACAGGCCGCTTCCGGGACTTCGAC  
TTTGTGTCAGAGCGATTCTTGAACCCTGA

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GCTGAAGTGGGATAACCTTCTGCTGGATGCCAGGGATTCTTGAAGATCGCAGACTTTGG  
ACTCTGCAAGGAAGGGATCGGCTTCGGGGACCGGACTAGCACCTTCTGTGGCACCCTGGGA  
GTTCTTGGCTCCCGAGGTGCTGACCCAGGAGGCATACACAGGGCTGTGGACTGGTGGGG  
GCTGGGTGTGCTGCTCTACGAGATGCTGGTGGGTGAGTGCCCGTTCCAGGGGACACAGA  
GGAAGAGGTGTTTACTGCATCGTCAACATGGACGCCCCCTACCCCGGCTTTCTGTGCGT  
GCAAGGGCTTGAGTTCATTGAGAAGCTCCTCCAGAAGTGCCCGGAGAAGCGCCTCGGGGC  
GGGTGAGCAGGATGCCGAGGAGATCAAGGTCCAGCCATTCTTCAGGACCACCAACTGGCA  
AGCCCTGCTCGCCCGCACCATCCAGCCCCCTTTGTGCCTACCCTGTGTGGCCCTGCGGA  
CCTGCGCTACTTTGAGGGCGAGTTCACAGGGCTGCCGCTGCCCTGACCCACCTGCACC  
CCACAGCCTCCTCACTGCCCGCCAACAGGCCGCTTCCGGGACTTCGACTTTGTGTGTCAGA  
GCGATTCTTGAACCCTGAGGGCATCTCCTGGCACCTCTGTCCCTTCCCCACAGACTG  
TTAGAGCCTCTGCTCGTTCACCCGTGCGCCCTGCCTGGAGGTCCAGGCCTTGCTGGGTAC  
TTCTGAGCCCTTGGGATTCAAAGTGGCAGCCATGGGGCCACTGTTGTGGGCTTTGCTCAG

## FIGURE 2K

TGTCAGTGGGCAAAGTGTGTCCCTTCCCCCTCCAGCTCGCCCTCTTCTACCTCCCAGCGA  
GACCTGGCCCAGAAAGGGTGCCGAGCAAGGAGTGATATGGTTTGTCTTTTAAAGACTGG  
ACTTGCTTTATATTAAATTTGTAAAAGTG

SEQ ID NO: 14\_H19102\_H

GGTGGCAACATCCGGGGTCCCTGGGCCCCGAGGCTGGAAGAGCCTCTGGACAGGTTTGGGA  
ACCATCAGGTCAGATCTGGAAGAACTCTGGGAACACGGGGGCACCACTATCTGCACCGA  
GAATCCCTAAAGCCAGCCCCAGTACTGGTAGAGAAGCCTCTGCCAGAGTGGCCAGTGCCT  
CAGTTCATCAACCTCTTTCTACCAGAGTTTCCATTAGGCCCATTAGGGGGCAGCAGCAG  
CTGAAGATTTTAGGCCTCGTGGCTAAAGGCTCCTTTGGAAGTGTCTCAAGGTGCTAGAT  
TGCACCCAGAAAGCTGTATTTGCAGTGAAGGTGGTGCCCAAGGTAAAGGTCCTACAGAGG  
GATACCGTGAGGCAGTGCAAAGAGGAGGTTAGCATCCAGCGACAGATCAACCATCCCTTT  
GTACACAGCTTGGGGGACAGCTGGCAGGGAAAACGGCACCTTTTCATTATGTGTAGCTAC  
TGCAGCACAGATCTGTACTCCCTTTGGTCGGCTGTTGGCTGCTTTCCCTGAGGCTTCCATC  
CGTCTCTTTGCTGCCGAGTTGGTGCTGGTACTGTGTTATCTCCATGACTTGGGCATCATG  
CATCGAGATGTGAAGATGGAGAATATTCTTCTAGATGAACGAGGCCATCTGAAACTGACA  
GACTTTGGTCTGTCCCGCCACGTGCCCCAGGGAGCTCAAGCCTACACTATCTGTGGCACT  
CTTCAGTACATGGCCCCAGAGGTCTTAAGTGGAGGACCTTACAACCATGCTGCTGATTGG  
TGGTCCCTGGGTGTCTTGCTTTTCTCTCTGGCGACTGGAAAGTTTCCAGTGGCTGCAGAG  
AGAGATCATGTGGCCATGTTGGCAAGTGTGACCCACAGTGACTCTGAGATCCCAGCTTCT  
CTTAACCAGGGCCTCTCACTCCTGCTCCATGAGCTCTTATGCCAGAACCCCTCCATCGT  
CTACGTTATCTGCATCACTTCCAGGTCCACCTTTCTTTCTGGGGTGTGGCCTTCGACCCA  
GAGCTCCTACAGAAGCAGCCAGTGAACCTTTGTACGGAGACACAAGCTACCCAGCCCAGT  
TCAGCGGAGACCATGCCCTTTGACGACTTTGACTGTGATCTGGAGTCCTTCTTGCTCTAC  
CCTATCCCTGCTTGA

SEQ ID NO: 15\_AA476563\_H

ATGGAATTCCTTTAGGATAGACAGTAAGGATAGCGCAAGTGAACCTCCTGGGACTTGACTTT  
GGAGAAAAATTGTATAGTCTAAAATCAGAACCTTTGAAACCATTCCTTTACTCTTCCAGAT  
GGAGACAGTGCTTCTAGGAGTTTTAATACTAGTGAAAGCAAGGTAGAGTTTAAAGCTCAG  
GACACCATTAGCAGGGGCTCAGATGACTCAGTGCCAGTTATTTTCGTTTAAAGATGCTGCT  
TTTGATGATGTGAGTGGTACTGATGAAGGAAGACCTGATCTTCTTGTAATTTACCTGGT  
GAATTGGAGTCAACAAGAGAAGCTGCAGCAATGGGACCTACTAAGTTTACACAACTAAT  
ATAGGGATAATAGAAAATAAACTCTTGGAAGCCCCCTGATGTTTTATGCCTCAGGCTTAGT  
ACTGAACAATGCCAAGCACATGAGGAGAAAGGCATAGAGGAACTGAGTGATCCCTCTGGG  
CCCAAATCCTATAGTATAACAGAGAAACACTATGCACAGGAGGATCCCAGGATGTTATTT  
GTAGCAGCTGTTGATCATAGTAGTTTCAGGAGATATGTCTTTGTTACCCAGCTCAGATCCT  
AAGTTTCAAGGACTTGGAGTGGTTGAGTCAGCAGTAACTGCAAACAACACAGAAGAAAGC  
TTATTCGGTATTTGTAGTCCACTCTCAGGTGCTAATGAATATATTGCAAGCACAGACACT  
TTAAAAACAGAAGAAGTATTGCTGTTTACAGATCAGACTGATGATTTGGCTAAAGAGGAA  
CCAATTCTTTATTCCAGAGAGACTCTGAGACTAAGGGTGAAAGTGGTTTAGTGCTAGAA  
GGAGACAAGGAAATACATCAGATTTTGGAGACCTTGATAAAAAATTAGCACTAGCCTCC  
AGGTTTTACATCCCAGAGGGCTGCATTCAAAGATGGGCAGCTGAAATGGTGGTAGCCCTT  
GATGCTTTACATAGAGAGGGAATTGTGTGCCGCGATTTGAACCCAAACAACATCTTATTG  
AATGATAGAGGACACATTCAGCTAACGTATTTTAGCAGGTGGAGTGAGGTTGAAGATTCC  
TGTGACAGCGATGCCATAGAGAGAATGTACTGTGCCCCAGAGGTTGGAGCAATCACTGAA  
GAACTGAAGCCTGTGATTGGTGGAGTTTGGGTGCTGTCTCTTTGAACTTCTCACTGGC  
AAGACTCTGGTTGAATGCCATCCAGCAGGAATAAATACTCACACTACTTTGAACATGCCA  
GAATGTGTCTCTGAAGAGGCTCGCTCACTCATTCAACAGCTCTTGCAAGTTCAATCCTCTG

## FIGURE 2L

GAACGACTTGGTGCTGGAGTTGCTGGTGTGAAGATATCAAATCTCATCCATTTTTTACC  
CCTGTGGATTGGGCAGAACTGATGAGATGA

SEQ ID NO: 16\_AA626690\_H

ATGCTACCATTTCGCTCCTCAGGACGAGCCCTGGGACCGAGAAATGGAAGTGTTTCAGCGGC  
GGCGGCGCGAGCAGCGGCGAGGTAAATGGTCTTAAAATGGTTGATGAGCCAATGGAAGAG  
GGAGAAGCAGATTCTTGTCATGATGAAGGAGTTGTTAAAGAAATCCCTATTACTCATCAT  
GTTAAGGAAGGCTATGAGAAAGCAGATCCTGCACAGTTTGAGTTGCTCAAGGTTCTTGTT  
CAGGGGTCATTTGGAAAGGTTTTTCTTGTTAGAAAGAAGACCGGTCCTGATGCTGGGCAG  
CTCTATGCAATGAAGGTGTTAAAAAAGCCTCTTTAAAAGTTTCGAGACAGAGTTTCGGACA  
AAGATGGAGAGGGATATACTGGTGGAAGTAAATCATCCATTTATTGTCAAATTGCACTAT  
GCCTTTCAGACTGAAGGGAACTGTACTTAATACTGGATTTTCTCAGGGGAGGAGATGTT  
TTCACAAGATTATCCAAAGAGGTTCTGTTTACAGAGGAAGATGTGAAATTCTACCTCGCA  
GAACTGGCCCTTGCTTTGGATCATCTGCACCAATTAGGAATTGTTTATAGAGACCTGAAG  
CCAGAAAACATTTTGCTTGATGAAATAGGACATATCAAATTAACAGATTTTGACTCAGC  
AAGGAGTCAGTAGATCAAGAAAAGAAGGCTTACTCATTTTGTGGTACAGTAGAGTATATG  
GCTCCTGAAGTAGTAAATAGGAGAGGCCATTCCCAGAGTGCTGATTGGTGGTCATATGGT  
GTTCTTATGTTGAAATGCTTACTGGTACTCTGCCATTTCAAGGTAAAGACAGAAATGAG  
ACCATGAATATGATATTAAAAGCAAACTTGGAAATGCCTCAATTTCTTAGTGCTGAAGCA  
CAAAGTCTTCTAAGGATGTTATTCAAAGGAATCCAGCAAATAGATTGGGATCAGAAGGA  
GTTGAAGAAATCAAAGACATCTGTTTTTTGCAAATATTGACTGGGATAAATTATATAAA  
AGAGAAGTTCAACCTCCTTTCAAACCTGCTTCTGGAAGAACAGATGATACTTTTTGT  
GATCCTGAATTTACTGCAAAAACACCTAAAGATTCTCCCGGTTTGCCAGCCAGTGCAAAT  
GCTCATCAGCTCTTCAAAGGATTCAGCTTTGTTGCAACTTCTATTGCAGAAGAATATAAA  
ATCACTCCTATCACAAGTGCAAATGTATTACCAATTGTTTCAGATAAATGGAAATGCTGCA  
CAATTTGGTGAAGTATATGAATTGAAGGAGGATATTGGTGTGGCTCCTACTCTGTTTGC  
AAGCGATGCATACATGCAACTACCAACATGGAATTTGCAGTGAAGATCATTGACAAAAGT  
AAGCGAGACCCCTCAGAAGAGATTGAAATATTGATGCGCTATGGACAACATCCCAACATT  
ATTACTTTGAAGGATGTCTTTGATGATGGTAGATATGTTTACCTTGTTACGGATTTAATG  
AAAGGAGGAGAGTTACTTGACCGTATTCTCAAACAAAAATGTTTCTCGGAACGGGAGGCT  
AGTGATATACTATATGTAATAAGTAAGACAGTTGACTATCTTCATTGTCAAGGAGTTGTT  
CATCGTGATCTTAAACCTAGTAATATTTTATACATGGATGAATCAGCCAGTGACAGATTCA  
ATCAGGATATGTGATTTTGGGTTTGCAAAACAACTTCGAGGAGAAAATGGACTTCTCTTA  
ACTCCATGCTACACTGCAAACTTTGTTGCACCTGAGGTTCTTATGCAACAGGGATATGAT  
GCTGCTTGTGATATCTGGAGTTTAGGAGTCCTTTTTTACACAATGTTGGCTGGCTACACT  
CCATTTGCTAATGGCCCCAATGATACTCCTGAAGAGATACTGCTGCGTATAGGCAATGGA  
AAATTCTCTTTGAGTGGTGGAACTGGGACAATATTTTCAGACGGAGCAAAGGATTTGCTT  
TCCCATATGCTTCATATGGACCCACATCAGCGGTATACTGCTGAACAAATATTAAAGCAC  
TCATGGATAACTCACAGAGACCAGTTGCCAAATGATCAGCCAAAGAGAAAATGATGTGTCA  
CATGTTGTTAAGGGAGCAATGGTTGCAACATACTCTGCCCTGACTCACAAGACCTTTCAA  
CCAGTCCTAGAGCCTGTAGCTGCTTCAAGCTTAGCCCAGCGACGGAGCATGAAAAAGCGA  
ACATCAACTGGCCTGTAA

SEQ ID NO: 17\_AA215680\_H

ATGAGCCTGGTGGCCTGTGAGTGCCTGCCCAGCCCCGGCCTGGAGCCTGAGCCTTGCTCA  
CGAGCACGGTCCCAAGCTCACGTGTACCTGGAGCAGATTTCGCAACAGGGTGGCTCTGGGA  
GTGCTTGACATGACAAAACGTGACTATCTGGTGGATGCGGCCACGCAGATCCGGCTGGCC  
CTGGAGCGGATGTTAGTGAGGACTATGAGGCGGCCTTCAACCACTATCAGAATGGCGTG  
GACGTGCTGCTCCGTGGCATAACGTTGACCCCAACAAGGAGCGACGTGAGGCTGTGAAG  
CTGAAAATTACCAAATACCTGCGGCGGGCAGAGGAGATCTTCAACTGCCACCTGCAGCGG

## FIGURE 2M

CCGCTGAGCAGTGGAGCCAGCCCCAGCGGGGTTTCAGCAGCCTGAGGCTCCGGGCCATT  
CGCACGCTGAGCTCTGCCGTGGAGCAGCTGAGGGGCTGCAGGGTGGTCGGGGTCATCGAG  
AAGGTGCAGCTGGTCCAGGACCCGGCAACCGGAGGGACCTTTGTGGTGAAGAGCCTACCC  
AGGTGCCACATGGTGAGCAGGGAGCGGCTGACCATCATCCACACGGAGTCCCCTACATG  
ACGAAGCTGCTCAGGTACTTTGTGAGCGAGGACTCCATCTTCCTGCACCTGGAGCATGTG  
CAAGGAGGCACTCTCTGGTCCCACCTGCTCTCCAGGCGCACTCCCGACATTCTGGGCTC  
AGCTCTGGCTCTACCCAGGAGAGGATGAAGGCTCAGCTCAACCCCCACCTCAACCTCCTG  
ACCCAGCGAGGCTTCCCTCAGGCCATGCCCTGGCCAGGACAGAATCGCCCTGGAGCCT  
CCTAGGACTTCTCCGAACCTTCTCCTAGCTGGGGAGGCCCCATCCACCAGACCCAGAGG  
GAGGCTGAAGGTGAACCCACAGCCAGGACCAGCACCTCTGGCTCCTCGGACCTTCCAAAG  
GCCCCAGGTGGCCACCTGCACCTTCAAGCTAGGAGGGCTGGCCAGAACTCAGACGCTGGG  
CCCCCTCGGGGGCTCACTTGGGTTCCTGAGGGGGCCGGCCCGGTGCTAGGGGGCTGTGGC  
CGAGGCATGGATCAGAGCTGCCTGTCAGCAGATGGGGCCGGCCGGGGCTGTGGCAGGGCC  
ACCTGGAGTGTGAGAGAGGAGCAGGTGAAGCAGTGGGCGGCAGAGATGCTGGTAGCGCTG  
GAGGCGCTGCACGAGCAGGGGGTGCTGTGCCGGGACCTCCACCCCGGGAACCTGCTCCTG  
GACCAGGCAGGTACATCCGGCTCACATATTTTGGCCAGTGGTCAGAGGTGGAGCCCCAG  
TGCTGCCGGGAGGCCGTGGACAATCTCTACAGCGCCCCAGAGGTGGGTGGGATTTCCGAG  
CTGACGGAAGCCTGTGACTGGTGGAGCTTTGGGTCTCTACTGTATGAACTGCTGACGGGA  
ATGGCACTGTCCCAGAGCCACCCTTCAGGAATCCAGGCCACACCCAGCTCCAGCTGCCC  
GAGTGGCTCAGTCGCCAGCGGCTCTCTGCTGACTGAGCTGCTGCAGTTCGAGCCTACC  
CGGCGCCTGGGCATGGGAGAAGGTGGTGTACGAAACTCAAGTCCCATCCCTTTTTCAGT  
ACCATCCAATGGAGCAAGCTGGTGGGGTAA

SEQ ID NO: 18\_SGK\_H

ATGACGGTGAAAAGTGAAGGCTGCTAAGGGCACCTCACTTACTCCAGGATGAGGGGCATG  
GTGGCAATTCTCATCGCTTTCATGAAGCAGAGGAGGATGGGTCTGAACGACTTTATTTCAG  
AAGATTGCCAATAACTCCTATGCATGCAAACACCTGAAGTTCAGTCCATCTTGAAGATC  
TCCCAACCTCAGGAGCCTGAGCTTATGAATGCCAACCTTCTCCTCCACCAAGTCCTTCT  
CAGCAAATCAACCTTGGCCCCGTCGTCCAATCCTCATGCTAAACCATCTGACTTTCACTTC  
TTGAAAGTGATCGGAAAGGGCAGTTTTTGGAAAGGTTCTTCTAGCAAGACACAAGGCAGAA  
GAAGTGTTCTATGCAGTCAAAGTTTTACAGAAGAAAGCAATCCTGAAAAAGAAAGAGGAG  
AAGCATATTATGTCGGAGCGGAATGTTCTGTTGAAGAATGTGAAGCACCTTTTCTGGTG  
GGCTTCACTTCTCTTTCCAGACTGCTGACAAATTGTACTTTGTCTAGACTACATTAAT  
GGTGGAGAGTTGTTCTACCATCTCCAGAGGGAACGCTGCTTCTGGAACCACGGGCTCGT  
TTCTATGCTGCTGAAATAGCCAGTGCCTTGGGCTACCTGCATTCACTGAACATCGTTTAT  
AGAGACTTAAAACCAGAGAATATTTTGGCTAGATTACAGGGACACATTGTCCTTACTGAT  
TTCGACTCTGCAAGGAGAACATTGAACACAACAGCACAAATCCACCTTCTGTGGCAGC  
CCGAGTATCTCGCACCTGAGGTGCTTCATAAGCAGCCTTATGACAGGACTGTGGACTGG  
TGGTGCCTGGGAGCTGTCTTGTATGAGATGCTGTATGGCCTGCCGCCTTTTTATAGCCGA  
AACACAGCTGAAATGTACGACAACATTCTGAACAAGCCTCTCCAGCTGAAACCAAATATT  
ACAAATTCGCAAGACACCTCCTGGAGGGCCTCCTGCAGAAGGACAGGACAAAGCGGCTC  
GGGGCCAAGGATGACTTCATGGAGATTAAGAGTCATGTCTTCTTCTCCTTAATTAAGTGG  
GATGATCTCATTAATAAGAAGATTACTCCCCCTTTTAACCCAAATGTGAGTGGGCCAAC  
GAGCTACGGCACTTTGACCCCGAGTTTACCGAAGAGCCTGTCCCCAACTCCATTGGCAAG  
TCCCCTGACAGCGTCTCGTCACAGCCAGCGTCAAGGAAGCTGCCGAGGCTTTCCTAGGC  
TTTTCTATGCGCCTCCCACGGACTCTTTCCTCTGA

SEQ ID NO: 19\_AA107515\_M

CGGGTCGACCCACGCGTCCGCCGGTTTCACTGCTCCCCTCAGTCTCTTTTGGGCTCTTTC  
CGGGCATCGGGACGATGACCGTCAAAGCCGAGGCTGCTCGAAGCACCTTACCTACTCCA



[illegible]

SEQ ID NO: 20\_AA109508\_M  
CCACCTGCAGCGGGAGCGCCGGTTCCTGGAGCCCCGGGCCAGGTTCTACGCTGCTGAGGT  
GGCCAGCGCCATTGGCTACCTGCACTCCCTCAACATCATTTACAGGGATCTGAAACCAGA  
GAACATTCTCTTGGACTGCCAGGGACACGTGGTGTGACGGATTTTGGCCTCTGCAAGGA  
AGGTGTAGAGCCTGAAGACACCACATCCACATTCTGTGGTACCCCTGAGTACTTGGCACC  
TGAAGTGCTTCGGAAAGAGCCTTATGATCGAGCAGTGGACTGGTGGTGTCTGGGGGCAGT  
CCTCTACGAGATGCTCCATGGCCTGCCGCCCTTCTACAGCCAAGATGTATCCCAGATGTA  
TGAGAACATTCTGCACCAGCCGCTACAGATCCCCGGAGGCCGGACAGTGGCCGCTGTGA  
CCTCCTGCAAAGCCTTCTCCACAAGGACCAGAGGCAGCGGCTGGGCTCCAAAGCAGACTT  
TCTTGAGATTAAGAACCATGTATTCTTCAGCCCCATAAACTGGGATGACCTGTACCACAA



FIGURE 20

GAGGCTAACTCCACCCTTCAACCCAAATGTGACAGGACCTGCTGACTTGAAGCATTTTGA  
CCCAGAGTTCACCCAGGAAGCTGTGTCCAAGTCCATTGGCTGTACCCCTGACACTGTGGC  
CAGCAGCTCTGGGGCCTCAAGTGCATTCTGGGATTTTCTTATGCGCCAGAGGATGATGA  
CATCTTGGATTGCTAGAAGAGAAGGACCTGTGAACTACTGAGGCCAGCTGGTATTAGTA  
AGGAATTACCTTCAGCTGCTAGGAAGAGCGACTCAAATAACAATGGCTTCAACGAGAAG  
CAGGTTTATTTTTTCCAGCACATAAAAGAAAAATAATGTTTCGGAGTCCAGGACTGGCAG  
GACAGGTCATCAGATACTCAGAGGCTGTATCTCTGCCCTGCCAACCTTGACAAATGGCTT  
CCAATGTTAGGTTTGCTACAAGATGGTTACTGGAGCTCTAGCTGCCTATTTTGTGTTTAG  
GGAAGGGAAAATGGAGGAAGGGGAGAAGAGCAAAGGGCGCTTTTAAAGAGCTTTCCCAA  
AAGCTCCACCCAATGACTTCTGCTTCCATCTCACTAACCACCCACCCCTACCTGGAATGG  
AGGCTGGGAGATGTGGCTTATTTGCTGGGTACGTGACTATCCCTAATAACAAAGGGGTTT  
TGACACTAAGACATTAGGGGAGAATGTTGGGTAGGCAGCCAGCACTCTTTTACCAGAGGG  
CCTCTGGTGTGTTGGATTTTGATCTCAATGTGTAAATGACAGAGATGTAACAAGCTCAT  
AGGGTATCAATATCTCTTATTGTTCT

SEQ ID NO: 21\_AA887783\_H  
CGGATGCATTTNTTGGTGTGCTCTTGAGGGATTAAATGCAAAGAGATCACACCATGGACT  
ACAAGGAAAGCTGCCCCAAGTGTAAGNATTCCCAGCTCCGATGAACACAGAGAGAAAAAGA  
AGAGGTTTACTGTTTATAAAGTTCTGGTTTCAGTGGGAAGAAGTGAATGGTTTGTCTTCA  
GGAGATATGCAGAGTTTGATAAACTTTATAACACTTTAAAAAACAGTTTCTGCTANGG  
CCCTGAAGATTCTGCCAAGAGAATATTTGGTGATAATTTTGATCCAGATTTTATTAAAC  
AAAGACGAGCAGGACTAAACGAATTCATTGAGAACCTAGTTAGGTATCCAGAACTTTATA  
ACCATCCAGATGTCAGAGCATTCCTTCAAATGGACAGTCCAAAACACCAAGTCAGATCCAT  
CTGAAGATGAGGATGAAAGAAGTTCTCAGAAGCTACACTCTACCTCACAGAACATCAACC  
TGGGACCGTCTGGAAATCCTCATGCCAAACCACTGACTTTGATTTCTTAAAGTTATTG  
GAAAAGGCAGCTTTGGCAAGGTTCTTCTTGCAAAACGGAACTGGATGGAAATTTTATG  
CTGTCAAAGTGTTACAGAAAAAATAGTTCTCAACAGAAAAGAGCAAAAACATATTATGG  
CTGAACGTAATGTGCTCTTGAAAAATGTGAAACATCCGTTTTTGGTTGGATTGCATTATT  
CCTTCCAAACAACCTGAAAAGCTTTATTTTGTCTGGATTTTGTAAATGGAGGGGAGGGAC  
ATGTTGTCTTAACAGATTTTGGGCTTTGTAAAGAAGGAATTGCTATTTCTGACACCACTA  
CCACATTTTGTGGGACACCAGAGTATCTTGACCTGAAGTAATTAGAAAACAGCCCTATG  
ACAATACTGTAGATTGGTGGTGCCTTGGGGCTGTTCTGTATGAAATGCTGTATGGATTGC  
CTCCTTTTTATTGCCGAGATGTTGCTGAAATGTATGACAATATCCTTCACAAACCCCTAA  
GTTTGAGGCCAGGAGTGAGTCTTACAGCCTGGTCCATTCTGGAAGAACTCCTAGAAAAG  
ACAGGCAAAATCGACTTGGTGCCAAGGAAGACTTTCTTGAAATTCAGAATCATCCTTTTT  
TTGAATCACTCAGCTGGGCTGACCTTGTAACAAAAGAAGATTCACCACCATTTAATCCTA  
ATGTGGCTGGACCAGATGATATCAGAACTTTGACACAGCATTTACAGAAGAAACAGTTC  
CATATTCTGTGTGTGTATCTTCTGACTATTCTATAGTGAATGCCAGTGTATTGGAGGCAG  
ATGATGCATTCGTTGGTTTCTCTTATGACCTCCTTCAGAAGACTTATTTTGTGAGCAG  
TTTGCCATTTCAGAAACCATTTGAGCAAAATAAGTCTATAGATGGGACTGAACTTCTATTT  
GTGTGAATATATTCAAATATGTATAACTAGTGCCTCATTTTTTATATGTAATGATGAAAAC  
TATGAAAAAATGTATTTTCTTCTATGTGCAAGAAAAATAGGGCATTTCAAAGAGCTGTTT  
TGATTAAAATTTATATTCTTGTTTAAATAAGCTTATTTTAAACAATTTAAAAGCTATTAT  
TCTTAGCATTAACCTATTTTTTAAAGAAACCTTTTTTGCTATTGACTGTTTTTCCCTCTA  
AGTTTACACTAACATCTACCCAAGATAGACTGTTTTTAAACAGTCAATTTAGTTCAGCT  
AACATATATTAATACCTTTGTAACCTCTTTGCTATGGCTTTTGTATCACACCAAACTAT  
GCAATTGGTACATGGTTGTTTAAAGAAGAAACCGTATTTTTCCATGATAAATCACTGTTTG  
AAATATTTGGTTCATGGTATGATCGAAATGTAAAAGCATAATTAACACATTGGCTGCTAG  
TTAACAATTGGAATAACTTTATTCTGCAGATCATTTAAGAAGTAACAGGCCGGCGCGGT  
GGCTCACGCCTGTAATCCAGCACTTTGGGAGGCTGAGGCGGGCAGATCACCTGAGGTCA

## FIGURE 2P

GGAGTTGGAGACCAGCCTGACCAACATGGACAAACCCCGTCTCTACTAAAAATACAAAAT  
TGGCAGGGTGTGGTGGCACATGCCTATAATCCCAGCTACTTGGGAGGCTAAGGCAGGAGA  
ATCGCTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCCGAGATCGCACCATTGCACTCCTG  
CCTGGGCAACAAGAGTGAAACTCCATCTCC

SEQ ID NO: 22\_R47805\_H

ATGGCGCACCAAACGGGCATCCACGCCACGGAAGAGCTGAAGGAATTCTTTGCCAAGGCA  
CGGGCTGGCTCTGTGCGGCTCATCAAGGTTGTGATTGAGGACGAGCAGCTCGTGCTGGGT  
GCCTCGCAGGAGCCAGTAGGCCGCTGGGATCAGGACTATGACAGGGCCGTGCTGCCACTG  
CTGGACGCCCAGCAGCCCTGCTACCTGCTCTACCGCCTCGACTCACAGAATGCTCAGGGC  
TTCGAATGGCTCTTCCCTCGCCTGGTGCCTGATAACTCCCCCGTGGCGCTGAAGATGCTG  
TACGCGGCCACGCGGGCCACAGTGAAAAAGGAGTTTGGAGGTGGCCACATCAAGGATGAG  
CTCTTCGGGACTGTGAAGGATGACCTCTCTTTTGTGGGTACCAGAAACACCTGTCTGCTCC  
TGTGCGGCACCTGCCCCGCTGACCTCGGCTGAGAGAGAGCTCCAGCAGATCCGCATTAAC  
GAGGTGAAGACAGAGATCAGTGTGGAAAGCAAGCACCAGACCCCTGCAGGGCCTCGCCTTC  
CCCCCTGCAGCCTGAGGCCAGCGGGCACTCCAGCAGCTCAAGCAGAAAATGGTCAACTAC  
ATCCAGATGAAGCTGGACCTAGAGCGGGAAACCATTGAGCTGGTGCACACAGAGCCCACG  
GATGTGGCCCAGCTGCCCTCCCGGGTGGCCCGAGATGCTGCCCGCTACCACTTCTTCCTC  
TACAAGCACACCCATGAGGGCGACCCCTTGAGTCTGTAGTGTTTCTACTTCCATGCCG  
GGGTACAAGTGCAGCATCAAGGAGCGAATGCTCTACTCCAGCTGCAAGAGCCGCCTCCTC  
GACTCCGTGGAGCAGGACTTCCATCTGGAGATCGCCAAGAAAATTGAGATTGGCGATGGG  
GCAGAGCTGACGGCAGAGTTCTCTACGACGAGGTGCACCCCAAGCAACACGCCTTCAAG  
CAGGCCTTCGCCAAGCCCAAGGGCCAGGGGGCAAGCGGGGCCATAAGCGCCTCATCCCG  
GGCCCGGTGAAAATGGGGATGACAGCTAG

SEQ ID NO: 23\_H60215\_H

CCACGCGTCCGGCGCCGCAGCCATGGAGGGAGGCGGGCGGCGGCGGCGGCGGCTCGGG  
TGGCTGCGCTGGGAGGCGGCGGTGAGAGGCTCGCACGCCTCCAGCCCGGCCCGCCCCC  
CGGGAGGGAGAGCCGAGCAGCCCCGGCTCTGGGCTACGGACTATGGGCGAATAGCTCTGA  
CCACCCGGCGAAGTGCACACACCCAGAAGCTATGTCCTTCGGCAGTAAAAGTTTACAGC  
ACAATATATGTGCTCTGCTCTCCTCCCGCAATCCTGCTCCAAGAGATCTTAAGCTGGAGG  
CACCAGGTCTGAATTCCAGACTCCTCCCCACCACTTCACTTCACTTCACTTCACTTCACT  
GACCACAGACCCATTGAGGGAGGCTGGCGGACTCTTCATCCTGGACAGTCCCTTACTGTA  
TGTCAAAGCTGAGAATGAAGCGGAGAGCATCAGACAGAGGAGCTGGGGAAACGTCGGCCA  
GGGCCAAGGCTCTAGGAAGTGGGATTTCTGGAAATAATGCAAAGAGAGCTGGACCATTCA  
TCCTTGGTCCCGTCTGGGCAACTCACCGGTGCCAAGCATAGTGCAGTGTTTGGCGAGGA  
AAGATGGCACGGATGACTTCTATCAGCTGAAGATCCTGACCCTGGAGGAGAGGGGGACC  
AAGGCATAGAGAGCCAGGAAGAGCGGCAGGGCAAGATGCTGCTGCACACCGAGTACTCAC  
TGCTGTCTCTCCTGCACACGCAGGATGGCGTGGTGCACCACCACGGCCTCTTCCAGGACC  
GCACCTGTGAAATCGTTGAGGACACAGAATCCAGCCGGATGGTTAAGAAGATGAAGAAGC  
GCATCTGCCTCGTCCCTGGACTGCCTCTGTGCTCATGACTTCAGCGATAAGACCGCTGACC  
TCATCAACCTGCAGCACTACGTTCATCAAGGAGAAGAGGCTCAGCGAGAGGGAGACTGTGG  
TAATCTTCTACGACGTGGTCCGCGTGGTGGAGGCCCTGCACCAGAAAAATATCGTGACA  
GAGACCTGAAGCTGGGGAACATGGTGTCTCAACAAGAGGACACATCGGATAACCATCACCA  
ACTTCTGCCTCGGGAAGCATCTGGTGAGCGAGGGGGACCTGCTGAAGGACCAGAGAGGGA  
GCCCTGCCTACATCAGTCCCGACGTGCTCAGCGGCCCGGCGTACCGTGGCAAGCCAGTG  
ACATGTGGGCCCTGGGCGTGGTGTCTTACCATGCTGTATGGCCAGTTCCCTTCTACG  
ACAGCATCCCGCAGGAGCTCTTCCGCAAGATCAAGGCTGCCGAGTATACCATTCTGAGG  
ATGGACGGGTTTCTGAGAACACCGTGTGTCTCATCCGGAAGCTGCTGGTCTTGAACCC  
AGCAGCGCCTGGCCGCCCGCCGACGTCCTGGAGGCCCTCAGTGCCATCATTGCATCATGGC

FIGURE 2Q

AGTCCCTGTCATCTCTGAGTGGGCCTTTGCAAGTGGTTCCTGACATTGATGACCAAATGA  
GCAATGCGGATAGCTCCCAGGAGGCGAAGGTGACGGAGGAGTGCTCCCAGTACGAGTTTG  
AGAATAACATGCGTCAGCAGCTGCTGCTGGCCGAGGAGAAGAGCTCCATCCATGACACCC  
GGAGCTGGGTACCCAAGCGGCAGTTCGGCAGCGCACCACCGGTGCGACGGCTGGGCCACG  
ACGCACAGCCCATGACCTCCTTGGACACGGCCATCCTGGCGCAGCGCTACCTGCGGAAAT  
AACAGCCTCAGCCGGGGCCACCAGCACTGCTGCCACTTCTTCCAGCCCCAGCCAAAGGCG  
TGGCTGTCAGGGCTGGGCCCTGTAGTGCTGGACTCTCCCGGGCCACAATAGGGACAGGGC  
AGGGACAGGGACAGCCAGGTACACGTGGGGTCAGCAGAGGTACCACGAAGCTACCTTT  
TGGGATGATTGCTCGATTGTTTGGTTTTTAAATCTGAGAAGCCTAGATAACTAATCTGCT  
TTTAATCACGATGTTTAAATCTACCTCTGTCTCTTTAACCATGCTGTCTCTGGACTGAGC  
AAGAGGGAGGAGGGAGCCTGCTACCCCACTCCAGGGCCTTCCCCAGCGGCCACCAACTG  
ACCTGGGGCGCTGCTCCCCACAGTCCAAATAAGCTGAAAAGTGCAGCTCGCTGCAGGCCCC  
AGAGCGAGCTTCCCCCTCCTCCTGCTCTCCAGGCCCTGCCACAGCCTCTTTCCGTCCC  
TCTCTTTCTGATCCAGGCCCTCAGTCCAAGCTTTGGAAAACCTTCACCTCATCTTAAAC  
CAAAC TCAAATATATTTATTTTTTTTACCAT

SEQ ID NO: 24\_SGK324\_H

CGCCGATGGCCAGCACCAGGAGTATCGAGCTGGAGCACTTTGAGGAACGGGACAAAAGG  
CCGCGGCCGGGGTCGCGGAGAGGGGGCCCCAGCTCCTCCGGGGGCAGCAGCAGCTCGGGC  
CCCAAGGGGAACGGGCTCATCCCCAGTCCGGCGCACAGTGCCCACTGCAGCTTCTACCGC  
ACGCGGACCCTGCAGGCCCTCAGCTCGGAGAAGAAGGCCAAGAAGGCGCGCTTCTACCGG  
AACGGGGACCGCTACTTCAAGGGCCTGGTGTTTGCCATCTCCAGCGACCGCTTCCGGTCC  
TTCGATGCGCTCCTCATAGAGCTCACCCGCTCCCTGTCCGACAACGTGAACCTGCCCCAG  
GGTGTCCGCACTATCTACACCATCGACGGCAGCCGGAAGGTCAACAGCCTGGACGAGCTG  
CTGGAAGGTGAGAGTTACGTGTGTGCATCCAATGAACCATTTCGTAAAGTCGATTACACC  
AAAAATATTAATCCAAACTGGTCTGTGAACATCAAGGGTGGGACATCCCAGCGCTGGCT  
GCTGCCTCCTCTGTGAAAAGTGAAGTAAAAGAAAGTAAAGATTTTCATCAAACCCAAGTTA  
GTGACTGTGATTGCAAGTGGAGTGAAGCCTAGAAAAGCCGTGCGGATCCTTCTGAATAAA  
AAGACTGCTCATTCTTTGAACAAGTCTTAACAGATATCACCGAAGCCATTAAACNAGCC  
TCAGGAGTCGTCAAGAGGCTCTGCACCCTGGATGGAAAGCAGGTGAGAGTTACGTGTGTG  
CATCTGCCAGACTTTTTTGGTGATGACGATGTTTTTATTGCATGTGGACCAGAAAAATTT  
CGTTATGCCAAGATGACTTTGTCTGGATCATAGTGAATGTCGTGCTCTGAAGTCATCT  
TATTCTCGATCCTCAGCTGTTAAGTATTCTGGATCCAAAAGCCCTGGGCCCTCTCGACGC  
AGCCAGATTTCTGCTCATGGCAGATCTTCTTCCAATGTAAACGGTGGACCTGAGCTTGAC  
CGTTGCATAAGTCTGAAGGTGTGAATGGAAACAGATGCTCTGAATCATCAACTCTTCTT  
GAGAAATACAAAATTGGAAAGGTCAATTGGTGATGGCAATTTTGAGTAGTCAAAGAGTGT  
ATAGACAGGTCCACTGGAAAGGAGTTTGCCCTAAAGATTATAGACAAAGCCAAATGTTGT  
GGAAAGGAACACCTGATTGAGAATGAAGTGTCAATACTGCGCCGAGTGAAACATCCCAAT  
ATCATTATGCTGGTTCGAGGAGATGGAAACAGCAACTGAGCTCTTCTGGTGATGGAATTG  
GTCAAAGGTGGAGATCTCTTTGATGCAATTACTTCGTGACCAAGTACACTGAGAGAGAT  
GGCAGTGCCATGGTGTACAACCTTAGCCAATGCCCTCAGGTATCTCCATGGCCTCAGCATC  
GTGCACAGAGACATCAAACCAGAGAATCTCTTGGTGTGTGAATATCCTGATGGAACCAAG  
TCTTTGAAACTGGGAGACTTTGGGCTTGCGACTGTGGTAGAAGGCCCTTTATACACAGTC  
TGTGGCACACCCACTTATGTGGCTCCARAAATCATTGCTGAAACTGGCTATGGCCTGAAG  
GTGGACATTTGGGCAGCTGGTGTGATCACATACATACTTCTCTGTGGATTCCCACCATTC  
CGAAGTGAGAACAACTCCAGGAAGATCTCTTCGACCAGATCTTGGCTGGGAAGCTGGAG  
TTTCCGGCCCCCTACTGGGATAACATCACGGAATCTGCCAAGGAATTAATCAGTCAAATG  
CTTCAGGTAAATGTTGAAGCTCGGTGTACCGCGGGACAAATCCTGAGTCACCCCTGGGTG  
TCAGATGATGCCTCCCAGGAGAATAACATGCAAGCTGAGGTGACAGGTAAACTAAAACAG  
CACTTTAATAATGCGCTCCCCAAACAGAACAGCACTACCACCGGGGTCTCCGTCTCATG

## FIGURE 2R

GTGAGTGGAAGGCGGCAGGTCTGGCCTGACTGCGGAGCCGGCCTTGAAGTTTTTGAATTA  
GGTAGCCGGGAGCTGCCCTCACATGGAAGTTGGTGCCTTCCGTAGTCCTATTTTCATATGA  
AGATTGGCTTGGCATGTGGAGGGCACTCATTCGGCAACTCCCAGGCTTTGGGCACTGTGT  
GGAGGGGCTTGTGTAGGGACCAGCAGGCCTGGTGTGAGGGGTCCAGGCGTCAAGGAGCTC  
CTGGCTGGGCCCTCTGGGCAGCTGCTTCCACTCTTGTCTCTGCCTTCTCATCTAGAGAGA  
CTCCCAAGCCCTGGAGGGGTGTGTTGTGTAGGAATTAACCTCCCTGCCTACCCCAAGGCC  
TCAGAAATAGATTATTAGAGATGTGAATTATTCTTTGAGACTTGGGATAAGAAACAGCCA  
AAGCTAAACATATTTTCACTTTTAAAAAATCAGTGTTTTTATAAAACACAGTTTGGGGCTTT  
TAAAGGTACATAATCAAGGAAAAAATATATATTCATTTTTCAGGGTTGGTAACATTTTA  
TGAGATGTCAGTGACAACGATGGCCTTATTTTTCAGCCTTTTCTTCTTCCAAAATGTT  
TCTTAAGGCAACTCTCCTAAATACATAAAACACAACAAATTAATGAAAAGTGACATGAG  
AGTAAATGAATCAAAAGGAAAAAACATTGAACCAGAGGTGAGGGCAGCACACCCGCAGCA  
GCTGTCCAGGCCTGAGCCAATGCAACCCTGGGCGGGAAGGCCAGCTCACCGTGAGCAGGT  
AGAAGCCAGCCAGCCACCCAGGCAGGGACCTTGGTTCTCCCCACACACTCCCAGGAGCAG  
GGAACAGGGGTGGAGTGGCCTTTCCCAGAGCTGGAGTTGGCTGCAGCAGCTTTCGAATCA  
GACCTGCCAAGGTGATGGGCGTCTGAGTTTACATCTGGGCCCCCGTGACCCCACTGAG  
TCCTGACAGCTAAGGATGGGCCACCTCCACAGCTCCGTCACTCGTACTTGGGACAGGCCT  
CTCATCCTCTGGGAAGGTCTCCTTGTTCCTACCCAACTAGAAGGGAACAGTGGCATA  
TTCTCATGGTACATGGTTGTCTGAAAGCCTTACCTAGGAAGACGCAGGGTCTAGATAGAA  
GCTATAAGGAAGCCACACACATAACCCACATCCCCACACCCCAACATCCCCACACTCC  
CCACACCCCCACACCCCCACATCCCCACCATAATTACCCCCACCTCCAAATATCTCAT

SEQ ID NO: 25\_W30246\_M SGK324\_M

ACCAAGTCCTCCAGCTCCTCTCCAACCAGCCCGGGAAGTTTCAGAGGATTGAAGATTTCT  
GCTCAGGGCAGATCTTCTTCCAACGTAAACGGTGGGCCTGAACTTGACCGTTGCCTGAGC  
CCTGAAGGTGTGAATGGAAACCGGTGCTCCGAGTCGTTCCCCCTTCTGGAGAAATACAGA  
ATAGGGAAGGTCAATCGGGGACGGCAACTTCGCGGTAGTTAAGGAGTGCGTGGACAGGTAC  
ACTGGAAGAGATTTGCATTAAAGATTATAGACAAAGCCAAATGCTGTGGAAGGAGCAT  
CTGATTGAGAACGAAGTGTCAATCCTGCGCCGAGTGAAGCACCCCAACATCATCATGTTG  
GTTGAAGAGATGGAAACAGCAACTGACCTCTTCTAGTGATGGAAGTGGTCAAAGGTGGA  
GATCTCTTTGATGCGATTACCTCTTCAACCAAGTACACTGAGAGAGATGGAAGCGCCATG  
GTGTACAACCTAGCCAATGCCCTCCGGTACCTGCACAGCCTCAGCATCGTCCACAGGGAC  
ATCAAGCCTGAGAATCTGCTGGTGTGCGAATACCCAGATGGAACCAAGTCTTTGAAGCTG  
GGAGACTTTGGGCTGGCGACGGTGGTTGAAGGCCCGTTGTACACGGTCTGTGGCACGCCA  
ACTTATGTGGCACCAGAGATCATAGCTGAAACAGGTTATGGCCTGAAGGTGGATGTTTGG  
GCAGCTGGTGTGATTACATACTTCTCTGTGGATTCCCACCATTCGGAGTGAGAAC  
AATCTCCAGGAAGATCTCTTTGACCAGATCTTGGCTGGAAAGCTGGAATTCACGCCCCC  
TACTGGGACAACATTACAGACTCTCCTTGTGTGTGTTTTAGGAAATGCTTATGAAGCTGG  
CCCGTGGGCTTCCCAGTGGGACGTGCAGCAGTTCTTGGCAGAGCAGGGCCAGCTCTGCTG  
TGTCATCTCCAGGGTCTCCCATCACCTCTGCTCTTGGCCATGGCAGGTCTGCTGAGACCC  
CGCGGGGACGGGGGCATGGTGCTCCCTGATTGGCCTGTGACCAACCTTCTGGAAGGCTGC  
TGGCAGTTTTCCCTGTTTTCCACCACCCCACTCTTTTAAATAATTGTATATACTGTACT  
TGTTCTACTTGCTTGTCTTTAAACAGGGGCCCCCACAGTTCACCTCTCACTGTAGATTT  
TGCCTTTTCCAGGTATCCCCAACCTGCAATAAACTCTTCCCTCTTCAG

SEQ ID NO: 26\_AA383293\_H

CCAGCAGCCAAGAGGGTAGTGGTGTACCGGAATGGGGACCCATTCTTCCCAGGCTCCCAG  
CTGGTGGTGAATCAACGCCGCTTCCCCACCATGGAGGCCTTCCCTCTGCGAGGTGACATCA  
GCTGTGCAGGCCCCACTGGCTGTGCGTGGCCTCTACACACCTTGTATGGCCACCCCTGTC  
ACCAACCTGGCAGACTTGAAGAACAGAGGGCAGTATGTGGCCGCTGGATTGAACGATTTC

## FIGURE 2S

CACAAGCTCCCCCTTACCAGGCTTTTTGTCTCAGTGTGTTTCAGGAATGGGGACCTGGTA  
AGTCCCCCATTTAGTCTGAAGCTGTCCAGGCTGCCAGCCAGGACTGGGAAACTGTGTTG  
AAGCTCCTGACTGAGAAGGTCAAGTTGCAGAGTGGGGCTGTGAGACTCTGCACCCTAGAG  
GGGCTCCCACTGTGAGCAGGGAAGGAGCTGGTAACTGGCCATTACTATGTGGCTGTCCGA  
GAGGATGAGTTCAAGGACCTTCCCTATCCAGCTCTGTCCACAAGAGGGCTCCTGGCAGCA  
GGCAATGAAGCCCACCTGAGGAGTGGAGTGGGGACTGTGCTGTTCCCCAAGCCTCTT  
GGAAGGAAGGCTAAGAAGGAGACATGCCTAATCGTGACCCTGACCCTGAAATACCAGCAG  
TCAGAAACAAGCAGAGACGGGCAATCATTCCCATCAGGAGTTATAGGAGTATATGGAGCT  
CCCCACCGAAGGAAGGAGACAGCGGGGGCCCTGGAAGTAGCAGATGATGAAGACACTCAG  
ACAGAGGAGCCCTTGGATCAGAGGGCAGCACAGATAGTGAACAGGTTACTTGTCTGCAA  
GACTTTTTTGGTGTATGACGATGTTTTTATTGCATGTGGACCAGAAAAATTTCTGTATGCC  
CAAGATGACTTTTGTCTGGATCATAGTCGTGACGGCTCCTGAGAGAGCACCAGGCGGGC  
TTTGAGAAGCTCCGCAGGACCCGAGGAGAAGAGAAGGAGGCAGAGAAGGAGAAAAAGCCA  
TGTATGTCTGGAGGCAGAAGGATGACTCTCAGAGATGACCAACCTGCAAAGCTAGAAAAG  
GAGCCCAAGACGAGGCCAGAAGAGAACAAGCCAGAGCGGCCAGCGGTGCGAAGCCACGG  
CCCATGGGCATCATTGCCGCCAATGTGGAAAAGCATTATGAGACTGGCCGGGTCTATTGGG  
GATGGGAACCTTTGTCTGTGCTGAAGGAGTGCAGACACCGCGAGACCAGGCAGGCCTATGCG  
ATGAAGATCATTGACAAGTCCAGACTCAAGGGCAAGGAGGACATGGTGGACAGTGAGATC  
TTGATCATCCAGAGCCTCTCTACCCCAACATCGTGAAATTGCATGAAGTCTACGAAACA  
GACATGGAAATCTACCTGATCCTGGAGTACGTGCAGGGAGGAGACCTTTTTGACGCCATC  
ATAGAAAGTGTGAAGTTCCCGGAGCCCGATGCTGCCCTCATGATCATGGACTTATGCAA  
GCCCTCGTCCACATGCACGACAAGAGCATTGTCCACCGGGACCTCAAGCCGGAACCTT  
TTGGTTTCAGCGAAATGAGGACAAATCTACTACCTTGAAATTGGCTGATTTTGGACTTGCA  
AAGCATGTGGTGAGACCTATATTTACTGTGTGTGGGACCCCAACTTACGTAGCTCCCGAA  
ATTCTTTCTGAGAAAGGTTATGGACTGGAGGTGGACATGTGGGCTGCTGGCGTGATCCTC  
TATATCCTGCTGTGTGGCTTTCCCCCATTCGCGAGCCCTGAXXGAGGGGACCAGGACGAG  
CTCTTTAACATCATCCAGCTGGGCCACTTTGAGTTTCTCCCCCTTACTGGGACAATATC  
TCTGATGCTGCTAAAGATCTGGTGAGCCGGTTGCTGGTGGTAGACCCCAAAAAGCGCTAC  
ACAGCTCATCAGGTTCTTCAGCACCCCTGGATCGAAACAGCTGGCAAGACCAATACAGTG  
AAACGACAGAAGCAGGTGTCCCCAGCAGCGATGGTCACTTCCGGAGCCAGCACAAGAGG  
GTTGTGGAGCAGGTATCATAGTCACCACCTTGGGAATCTGTCCAGCCCCAGTTCTGCTC  
AAGGACAGAGAAAAGGATAGAAGTTTGAGAGAAAAACAATGAAAGAGGCTTCTTCACATA  
ATTGGTGAATCAGAGGGAGAGACACTGAGTATATTTTAAAGCATATTAAAAAATTAAGT  
CAATGTTAAATGTCACAACATATTTTAGATTTGTATATTTAAAGCCTTTAATACATTTT  
TGGGGGGTAAGCATTGTCATCAGTGAGGAATTTTGGTAATAATGATGTGTTTTGCTTCCC  
CTTTGTAACCAAGTTTATTCTGTACTACAGGAGTGGTGCTTACCAGGGTCTAAACTCCCC  
CTGTGAGATTAATAAGGTGCATTG

SEQ ID NO: 28\_AA197883\_M

ATGCCAACCGCGCCGGTCCCTGCGCCCCGCCGCCGCCAGCGACCCCCGCCCGCCGGCA  
CCCAGTCGCCCTGCGCCTCCCATTCGGGGCCACCGAGGCCCATGTGACCATTCTCTGAAA  
TGCTTAAGCTCGAAGATCTCTGAGAGAAAGCTGCCAGGCCCTGGTTACCTGCGGGACGA  
GGACCTCTGGAGAAGCCAGTTCTGGGGCCACGTGGTGCCGTATGCCGCTGTTTCAGCCCT  
CAGAGCAGCCTCCACTCAGTCCGCGCAGAGCACAGCCCACTGAAGCCCAGGGTGGTGACG  
GTGGTGAAGCTGGGTGGGCAGCCCCCTCCGTAAGGCCACCCTGCTCCTCAACCGGCGCTCA  
GTGCAGACCTTTGAGCAGCTCCTATCAGACATCTCCGAAGCCTTGGGCTTCCACGCTGG  
AAGAACGACCGTGTGCGGAAGCTGTTACCCTCAAGGGCAGGGAGGTGAAGAGTGTGTCT  
GACTTCTTCCGGGAGGGTGATGCTTTCATAGCTATGGGCAAAGAGCCGCTGACATTGAAG  
AGTATCCAGTTGGCCATGGAGGAGCTGTATCCTAAGAACCGGGCTCTTGCCCTGGCCCCCT  
CACAGTAGAGTCCCCTCCCCAAGGCTGAGAAGCAGACTTCCCAGCAAGCTTCTGAAAGGA

## FIGURE 2T

AGTCACCGCTGTGGGGAGGCAGGAAGCTATAGCGCGGAAATGGAGAGTAAGGCAGTCTCT  
AGGCATCAGGGCAAGACTTCCACAGTGCTGGCCCCAGAAGACAAGGCGAGGGCCCAGAAG  
TGGGTAAAGAGGGAAACAGGAGTCAGAACCTGGTGGCCCCGCTTCACCCGGGGCAGCCACT  
CAGGAGGAGACTCATGCAAGTGGAGAGAAACATCTGGGGGTGGAGATCGAAAAGACCTCC  
GGGGAGATTGTCAGATGTGAGAAGTGTAAAGAGAGAAAGAGAGCTGCAGTTGGGCCTGCAG  
AGGGAGCCGTGCCCCGCTGGGAACCAAGAGCTGAGCTGGACCTGGGGAGAGCTCAGAAGAGGGAT  
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GGAGAGGAAGGGTGGAAAGGGTGACAGCCATCGGGGCAGTCCCAGGGACCCCCCTCAGGAA  
ATGAGGAGGCCCAACAGCAACTCAGACAAGAAAGAGATCAGAGGCTCAGAAAGTCAGGAC  
AGTTATCCTCAGGGGGCACCCAAGGCCCAGAAGGACTTCGTGGAAGGGCCACCAGCTGTA  
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AAGGAGTCTAAGAGGAAGCTAGAAGAGAAGAGGCCAGAACGACCCAGTGGCCGGAAGCCG  
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GCCATGAAGATGATTGACAAGTCCCAGCTGAAGGGTAAGGAGGACATTGTGACAGTGAG  
ATTTTAATCATCCAGAGTCTCTCTCATCCCAACATTGTGAAACTGCATGAGGTCTACGAA  
ACGGAGGCGGAGATCTACCTGATCATGGAGTATGTGCAGGGAGGGGACCTTTTTTGATGCC  
ATCGTTGAAAATGTGAAGTTTCCAGAGCCCGAGGCTGCAGTTATGATCACAGACTTGTGT  
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TCTGATGCTGCCAAAGATCTGGTGAGAAATTTGCTGGAGGTGGACCCTAAGAAGCGGTAC  
ACGGCCGAACAGGTCCTACAGCATCCCTGGATTGAGATGGTTGGGCATACCAACACAGGG  
AACTCACAGAAGGAGGAGTCCCCCAACAGTTTAGGTCACTTCCAGAGTCAGCACAAAGAAG  
GTTGCAGAGCAGATGCCATAA

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CTCCGCTGCTGTGCGCCAGGAGTCACTTCACGAGAAGCCAGGTCACAACCGTCGGGCCCTTG  
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GGGGGCAGTCCCGGGAGAACCTGCGGCGGCCGGAGCGGTAAAATAAGTGACTAAAGAAG  
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CGGGCAGAAATTTTACACGAGATTGCTGTGCTTGAATTGGCAAAGTCTTGTCCCCGTGTT  
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GCAGGTGGAGAAATTTTCAGCCTGTGTTTACCTGAGTTGGCTGAAATGGTTTCTGAAAAT  
GATGTTATCAGACTCATTAAACAAATACTTGAAGGAGTTTATTATCTACATCAGAATAAC  
ATTGTACACCTTGATTTAAAGCCACAGAATATATTACTGAGCAGCATATACCCTCTCGGG  
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GAAATCATGGGAACACCAGAATATTTAGCTCCAGAAATCCTGAACTATGATCCCATTACC  
ACAGCAACAGATATGTGGAATATTGGTATAATAGCATATATGTTGTTAACTCACACATCA  
CCATTTGTGGGAGAAGATAATCAAGAAACATACCTCAATATTTCTCAAGTTAATGTAGAT  
TATTCGGAAGAACTTTTTCATCAGTTTACAGCTGGCCACAGACTTTATTACAGGCCTT

FIGURE 2U

TTAGTAAAAAATCCAGAGAAAAGACCAACAGCAGAGATATGCCTTTCTCATTCTTGGCTA  
CAGCAGTGGGACTTTGAAAACCTGTTTTACCCTGAAGAACTTCCAGTTCCTCTCAAAC  
CAGGATCATTCTGTAAGGTCCTCTGAAGACAAGACTTCTAAATCCTCCTGTAATGGAAC  
TGTGGTGTAGAGAAGACAAAGAGAATATCCCAGAGGATAGCAGCATGGTTTCCAAAAGA  
TTTCGTTTTCGATGACTCATTACCCAATCCCCATGAACTTGTTTTAGATTGCTCTGTTAG  
CACTTTTTTCTTTGACTCATTGACTGAATTTGAAATTTTATATCCACTCCAGTGAGAT  
TATGATTTGTAGCTTCATATATGACATGTTTATATTGTAAATGCACCTTTCCATGGAATA  
ATTTAGGGAAGTGTTTTAATGTTAAATTACTAGTTGCTAGCATGTTATGATTTTCATATCC  
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GTGAAAG

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CCAGACGCGGCTGCACTTTTCAAACCTCAACTGTAAGAAGCGTCGGTCAGCGTCTGTGCG  
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GGAGATTGATTGCCGAAGTGTCTCAGGCTTGCTAACTACAACCCCTCAAACGCCGATTA  
AAACAGAGAATTTTAATAATTTCTATACTCTTACCCCAAAGAACTTTGGGAGAGGAAAAT  
TTGCTGTGGTTAGACAATGTATATCAAAATCAACTGGACAAGAGTATGCTGCCAAATCCC  
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TGGAGCTGGCCAGGTCTTGTCCCCACGTGATTAATCTGCATGAGGTCTACGAAAATGCAA  
CGGAAATCATTTTGGTGTAGAAATATGCTGCGGGTGGAGAAATTTTCAACCTGTGTTTAC  
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GAAAATTTGGGAATGCAAGTGAGCTTCGGGAAATCATGGGAACACCTGAATACTTAGCTC  
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ATCTGAATATTTCTCAAGTGAAATGTAGATTATTCAGAAGAAATGTTTTTCATCAGTTTCAC  
AGCTGGCCACAGACTTCATCCAGAGCCTTCTAGTAAAGAACCAGAGAAAAGACCAACAG  
CAGAATCCTGCCTATCCCACTCATGGCTGCAGCAGTGGGACTTTGGAAGCTTGTTTCATC  
CTGAGGAACTTCAGGCTCCTCTCAAATTCAGGATCTGACTCTCAGGTCTCTGAAGAGA  
AGACCTCCAAGTCCTCCTGTAATGGGAGCTGTGGAGCCCGGGAGGACAAGGAGAACATCC  
CTGAAGATGGCAGCTTAGTTTCTAAAAGATTTTCGATTCGATGACTCCTTGCCAGCCCCC  
ATGAACTTGTTCCAGATTTGTTCTGTGTAGCATTGTTCTCTGTGACTCATCTGGACTGACT  
CGGAAATTTGAAATCTCTGGTGTGAGATTGTGTTTGTAGCTTCATATATTATGTTTATAT  
TATAAATGCACTTCTGCTTAGAAGAACTTAAGGAACAGTTTAAATGCTAGGCTTCTGTTG  
GCTAGCATATCATTTCTTGTCTGAAATTGTTTTGCAGAGGAAAATATTTAAGTATATGA  
CAAAAAATGTAAATTGTGTTTAAGAGAACACATGCAACTGAAAGAACTCAAGTTCAGTCA  
GACTTATAAAATGGGTATATTATGGTTAGTAAAGTTGAAAAAAATGAAAACAGGAAT  
TTAGTAGGTTCTAAGGTAAAGCCCTATACCATAACTCTATTACAGAGAATCTGTTTGGGGA  
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TAGTTGAAAGTATTTCCAGTTACCAATAATAGCTTGAACTGTAAGATTTTCTTTGTGT  
GCCATGTGCTCGGTGAGAGGACACAGTCAACCAGAGCAGGGTTGATCCAGGCTGTTTCTC  
TGCAAACCGAGTCAAACTCGACATCATTTCCAGCTCATGTATTTTGTACGTGCATCATA  
TATCAGATCTAATAAGATCTGGAAGATGGATATGCAAATAAGAGGCCTTTGTCTTCTAGA  
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TTCATAAAGGGAAATGTTAAGTTCTGGCAGCTGACTTAGTGTTGGATGTCTCCTAAGTCT  
CAGGATAGAAGCCCATCATTAGAGCATAGGCACTTCAGGAATCTTGTGTGAAATTCTAG  
TGAGTGAGGAGGTGTGACATGCAGCTATCTTTGGGCTCCTTTTGTGTGTGTTCTGTGCTGGA  
CAACACATGGGAGTGTTCAAGTGTGTCCTGCTCAATATCTATGTTCAAGTCTGATGG



## FIGURE 2V

GAGGGGCTAGGGACTGCTTTGGAGATTTCCCACTGGTGTCATTTTAAGGTCTGTAATA  
ATGTCATGTTAAGATAACAGATCTCATAAATATGCTACTCTATCAGACTCCGTGCCAAA  
ACAAATTAAAAGCCTGTGTATTGAAGTGGGTGTTAGTCTAACAACCTGTAAATTCCTGAA  
ATTGTTACTAAAATTCCAAATCTTTAGATAACTTTAACTATTTAAATTGAGCATTGCT  
GTCTTTGTTTGATTAAAGGTTGAGTTCCTTTATATCTGTTATTTTAAAGGAAAAGTTGT  
TTGCCTTTTGATATGTGTGCATATGTGTATGTGTACAGGTATATGTATATATGTATT  
GATAGATAAAATACAGCCTTTAAACAACCTC

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ATGATCCCTTTGGAGAAGCCAGGCAGCGGGCTCCTCCCCAGGCGCCACCTCAGGCTCG  
GGCCGGGCGAGCCGGGGTCTGAGCGGGCCGTGCCGGCCGCCGCCGCCGCCAGGCCCCG  
GGGCTGCTGACAGAGATACGCGCCGTGGTGCGACCGAGCCCTTCAGGACGGCTACAGC  
CTGTGCCCCGGGCGGGAGCTGGGCAGGGGGAATTTGCAGTGGTGAGAAAATGTATAAAG  
AAAGATTCTGGGAAGAATTTGCTGCAAAGTTTCATGAGAAAAGAAGAAAAGGCCAAGAT  
TGTCGGATGGAAATAATTCATGAGATTGCTGTACTTGAAGTACACAAGACAATCCTTGG  
GTCATTAATTTACATGAAGTTTATGAGACTGCATCAGAAATGATCTTAGTTCTGGAATAT  
GCTGCTGGGGGTGAAATCTTTGACCAGTGTGTTGCAGACAGAGAAGAAGCCTTTAAAGAA  
AAAGATGTTCAAAGACTTATGCGACAGATTTTAGAAGGTGTTCACTTTTACACACTCGT  
GATGTAGTTCATCTTGATTTGAAGCCTCAGAATATTCTGTTGACAAGTGAATCTCCATTG  
GGTGACATTAAGATTGTTGATTTTGGCCTTCAAGAATATTGAAGAACAGTGAAGAGCTC  
CGAGAAATTATGGGTACCCCTGAATATGTGGCTCCTGAAATTCTTAGTTATGATCCTATA  
AGCATGGCAACAGATATGTGGAGCATTGGAGTGTAAACATATGTCATGCTTACAGGAATA  
TCACCTTTCTTAGGCAATGATAAACAAGAAACATTCTTAAACATCTCACAGATGAATTTA  
AGTTATTCTGAGGAAGAATTTGATGTTTTGTCTGAGTCGGCTGTTGATTTTCATCAGGACA  
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TTGACACAGAGCAGTATTCAAGAGCCTTCTTTCAGGATGGAAAAGGCACTAGAAGAAGCA  
AATGCCCTCCAAGAAGGTCATTCTGTGCCTGAAATTAATTCCGATACCGACAAATCAGAA  
ACCGAGGAATCCATTGTAACCGAAGAGTTAATTGTAGTTACTTCATATACTCTAGGACAA  
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GAGGAACCTTTGCTACAAGAAATTCAGGAGAATTTATCTACTGA

SEQ ID NO: 32\_AA021445\_H  
CGGGGCTGCCGGGGCGGGACTGGGGGAGCCGGGCCCCGCGGGCCGCCTGCTGCCTCCGCC  
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CACCATCGGCAAGGGCAACTTCGCGGTGGTCAAGCGGGCCACGCACCTCGTCACCAAGGC  
CAAGGTTGCTATCAAGATCATAGATAAGACCCAGCTGGATGAAGAAAATTTGAAGAAGAT  
GGTTATGGAGACAGAACGGATGATTTATCTGGTGACAGAATATGCTAGTGGAGGGGAAAT  
ATTTGACCACCTGGTGGCCCATGGTAGAATGGCAGAAAAGGAGGCACGTGGAAGTTCAA  
ACAGATCGTCACAGCTGTCTATTTTGTCACTGTGGAACATTGTTTCATCGTGATTTAA  
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AGCTGAATGCCAACAACTAAAGGAAGAAAGACAGGTGGACCCCTGAATGAGGATGTCTC  
CTTGGCCATGGAGGACATGGGACTGGACAAAGAACAGACACTGCAGTCATTAAGATCAGA



## FIGURE 2W

TGCCTATGATCACTATAGTGCAATCTACAGCCTGCTGTGTGATCGACATAAGAGACATAA  
AACCCTGCGTCTCGGAGCACTTCCTAGCATGCCCCGAGCCCTGGCCTTTCAAGCACCAGT  
CAATATCCAGGCGGAGCAGGCAGGTACTGCTATGAACATCAGCGTTCCCCAGGTGCAGCT  
GATCAACCCAGAGAACCAAATTGTGGAGCCGGATGGGACACTGAATTTGGACAGTGATGA  
GGGTGAAGAGCCTTCCCCCTGAAGCATTTGGTGGCTATTTGTCAATGAGGAGGCACACAGT  
GGGTGTGGCTGACCCACGCACGGAAGTTATGGAAGATCTGCAGAAGCTCCTACCTGGCTT  
TCCTGGAGTCAACCCCCAGGCTCCATTTCCTGCAGGTGGCCCCCTAATGTGAACCTTCATGCA  
CAACCTGTTGCCTATGCAAACTTGCAACCAACCGGGCAACTTGAGTACAAGGAGCAGTC  
TCTCTACAGCCGCCACGCTACAGCTGTTGAATGGAATGGGCCCCCTTGGCCGGAGGGC  
ATCAGATGGAGGAGCCAACATCCAACCTGCATGCCAGCAGCTGCTGAAGCGCCACGGGG  
ACCCTCTCCGCTTGTCAACATGACACCAGCAGTGCCAGCAGTTACCCCTGTGGACGAGGA  
GAGCTCAGACGGGGAGCCAGACCAGGAAGCTGTGCAGAGGTACTTGGCAAATAGGTCCAA  
AAGACATACTGGCCATGACCAACCCTACAGCTGAGATCCCACCGGACCTACAACGGCA  
GCTAGGACAGCAGCCTTTCCGTTCCCGGGTCTGGCCTCCTCACCTGGTACCTGATCAGCA  
TCGCTCTACCTACAAGGACTCCAACACTCTGCACCTCCCTACGGAGCGTTTCTCCCCTGT  
GCGCCGGTTCTCAGATGGGGCTGCGAGCATCCAGGCCTTCAAAGCTCACCTGGAATAAT  
GGGCAACAACAGCAGCATCAAACAGCTGCAGCAGGAGTGTGAGCAGCTGCAGAAGATGTA  
CGGGGGGCGAGATTGATGAAAGAACCCTGGAGAAGACCCAGCAGCAGCATATGTTATACCA  
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CCAGAGGTTAAGGATTCAGCCTTCAAGCCCCACCCCCAACCAACCAACCATCTCTT  
CAGGCAGCCCAGTAATAGTCTCCCCCATGAGCAGTGCCATGATCCAGCCTCACGGGGC  
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TGAGAACTGTTCTCTCTCCTCCCAACGTGGCACTAACCTGCTTGGGTATGCAGCAGCCTGC  
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AGGCACAGCTGCAGGCTCCAGTGGGCGCGGCATCTCCATCAGCCCCAGTGCTGGTCAGAT  
GCAGATGCAGCACCGTACCAACCTGATGGCCACCCTCAGCTATGGGCACCGTCCCTTGTC  
CAAGCAGCTGAGTGCTGACAGTGACAGAGGCTCACAGCTTGAACGTGAATCGGTTCTCCCC  
TGCTAACTACGACCAGGCGCATTTACACCCCCATCTGTTTTCCGACCAGTCCCGGGGTTCT  
CCCCAGCAGCTACAGCCCTTCAACAGGAGTGGGGTTCTCTCCAACCCAAGCCCTGAAAAGT  
CCCTCCACTTGACCAATTCCCCACCTTCCCTCCAGTGACATCAGCAGCCGCCACACTA  
TACCAGCTCGGCACTACAGCAGGCCCTGCTGTCTCCACGCGCCAGACTATAACAAGACA  
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CTCGGACATCCGGCTGCCCCCAACAGAGTTTGCACAGCTCATTAAGAGGCAGCAGCAACA  
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GAACCAAGGGGATGCGGGGAGTCTGGCTCCCAGCCTTGGGGGACAGAGCATGACAGAGCG  
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TGTGAGTCATGCCAAGAATTGGGGATACATCCCTATGGTCATCAGCCAACCTGCTGCATT  
CAGTAAAAATAAGGTGCCAGCAGAGAGCCTGTCTATAGGGAAGTGCATGGATAGAAGTTC  
TCCAGGACAAGCAGTGGAGCTGCCGGATCACAATGGGCTCGGGTACCCAGCACGCCCCCTC  
CGTCCATGAGCACCACAGGCCCCGGGCCCTCCAGAGACACCACACGATCCAGAACAGCGA  
CGATGCTTATGTACAGCTGGATAACTTGCCAGGAATGAGTCTCGTGGCTGGGAAAGCACT  
TAGCTCTGCCCGGATGTCCGATGCAGTTCTCAGTCAGTCTTCGCTCATGGGCAGCCAGCA  
GTTTCAGGATGGGGAAAAATGAGGAATGTGGGGCAAGCCTGGGAGGTCATGAGCACCAGA  
CCTGAGTGATGGCAGCCAGCATTTAAACTCCTCTTGCTATCCATCTACGTGTATTACAGA  
CATCTGCTCAGCTACAAGCACCCCGAAGTCTCCTTCAGCATGGAGCAGGCAGGCGTGTA

## FIGURE 2X

ACAAGAAACAGAGAGTTTTGTGTACAGCTTGGGAATGAAAAGGTTGATTGTAAACCCACA  
GTATCTAGCAGCGTTGTGCCAAATTGCCCTTGTGTTTCTCTCCACCCAAAATATCACAGC  
TGCTTTCCTCACATTTGGTTCATCCGTGTGCTGTTCTTTTGGGTTCTGAGAGGGTTTTGC  
CATGTTTGCTTGTATGACCAAGTCACCAAGGAAATAAACAGGAAGGAAATCCATGTTCTC  
C

SEQ ID NO: 33\_2R22-5-11\_H

CTGGGCCGCTGCCGGTCAGGTCGGCCGCCCTGACAGCTCCGGGAGCCTCAAGCGCGACA  
GGGCGCCCTCACCTCGGGACATCCACACACCGACCGCTCCTGCTCCAGAGGCAACAACCC  
AGCGCGCCTAGCCTGGCGCCGTGCAGCGAAGCCCAAGAGCTGGCCTCGCCACGAAGGTTG  
AACCAGCCAAATTTTCGAGACAGCTCACGGCTTAGAGGAAGGTTTCATCTAAATAAAGGCC  
GGCTAAAGTGACATTGCAGGGATTAAATCCTTCTTTGGCTGCCTGTGTGACCAGAAGGCT  
TATTTGCAAGTTTCTTCTTTCTGGGGTCCAGATTATTAGGTCTCCAGCGCCCTGCAGCT  
TGACAGAAAGAGAAGCATGAAATGAAGGTGAGAGATGAGATCCCGCAGCAGGGACGTGGG  
GGCCTCCAGGGGCATTTACGCACCAGAGTGCAAGATTCTCTGGCCATCAAGGGAAATAG  
CAAACAGAAGCCTTTGTCTGGGGCACAGCCACCTACCACAAAGCATCAGACTCCACGTC  
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ACAGCTAGAGCCTGCAAGTTCAACGTGAGGGAAGGTGGGAAATGTCTTGAGTGAGGCGAG  
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GCCGAGAGGGAGGCTGCTCAGCTCTCAGGAAAACCTCTTTTGAACCTGGGCACCTGCTGT  
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GACCAGAAAACCCAGAGGCTACTATCCCGAGAAATCTCCAGCATGGAAAAGCTGCACCAT  
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GAGTATGCAGGGGGTGGGGAGCTCTTCGGAAAAATTAGCACTGAGGGGAAGCTCTCTGAA  
CCAGAAAGCAAGCTCATCTTCTCCAGATTGTGTCTGCCGTGAAGCACATGCATGAAAAC  
CAAATTATTATAGAGATCTGAAAGCAGAAAATGTATTCTATACCAGTAATACTTGTGTG  
AAGGTGGGCGATTTTGGATTTCAGCACAGTAAGCAAAAAAGGTGAAATGCTGAACACTTTC  
TGTGGGTCTCCTCCCTACGCTGCGCCTGAACTCTTCCGGGACGAGCACTACATCGGCATT  
TACGTGGATATCTGGGCCTTGGGGGTGCTTTTGTACTTCATGGTGAAGTGGCACCATGCCA  
TTTCGGGCAGAAACCGTGGCCAAACTAAAAAAGAGCATCCTCGAGGGCACATACAGTGTA  
CCGCCGCACGTGTCAGAGCCCTGCCACCGACTCATCCGAGGAGTCCTTCAGCAGATCCCC  
ACGGAGAGGTACGGAATCGACTGCATCATGAATGATGAATGGATGCAAGGGGTGCCATAC  
CCTACACCTTTGGAACCTTTCCAACCTGGATCCCAAACATTTGTGCGAAACCAGCACTCTC  
AAGGAAGAAGAAAATGAGGTCAAAAGCACTTTAGAACATTTGGGCATTACAGAAGAGCAT  
ATTGAAATAACCAAGGGAGAGATGCTCGCAGCTCAATCACAGGGGTCTATAGAATTATT  
TTACATAGAGTCCAAAGGAAGAAGGCTTTGGAAAGTGTCCAGTCATGATGCTACCAGAC  
CCTAAAGAAAGAGACCTCAAAAAAGGGTCCCGTGTCTACAGAGGGATAAGACACACATCC  
AAATTTTGCTCGATTTTATAAATTGCACTAGACTGCTTGTAACCTAACCAAGATGATTGTT  
GCTGCTTCTAAATTTTTTCAAGGACAACCTTGAGTGGAGACATTTTTGTAAATTTTTAAAT  
AAACTTAAATTTGAGATATGCAAAAAAAA

SEQ ID NO: 34\_R31237\_1\_H, AAC33487

ATGTCCACTAGGACCCCATTTGCCAACGGTGAATGAACGAGACACTGAAAACCACACGTCA  
CATGGAGATGGGCGTCAAGAAGTTACCTCTCGTACCAGCCGCTCAGGAGCTCGGTGTAGA

## FIGURE 2Y

AACTCTATAGCCTCCTGTGCAGATGAACAACCTCACATCGGAACTACAGACTGTTGAAA  
ACAATCGGCAAGGGGAATTTTGCAAAAGTAAAATTGGCAAGACATATCCTTACAGGCAGA  
GAGGTTGCAATAAAAAATAATTGACAAAACCTCAGTTGAATCCAACAAGTCTACAAAAGCTC  
TTCAGAGAAGTAAGAATAATGAAGATTTTAAATCATCCCAATATAGTGAAGTTATTCGAA  
GTCATTGAAACTGAAAAAACACTCTACCTAATCATGGAATATGCAAGTGGAGGTGAAGTA  
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CAGATTGTGTCTGCAGTTCAATACTGCCATCAGAAACGGATCGTACATCGAGACCTCAAG  
GCTGAAAATCTATTGTTAGATGCCGATATGAACATTAAAAATAGCAGATTTCCGGTTTAGC  
AATGAATTTACTGTTGGCGGTAAACTCGACACGTTTGTGGCAGTCCTCCATACGCAGCA  
CCTGAGCTCTTCCAGGGCAAGAAATATGACGGGCCAGAAGTGGATGTGTGGAGTCTGGGG  
GTCATTTTATACACACTAGTCAGTGGCTCACTTCCCTTTGATGGGCAAAACCTAAAGGAA  
CTGAGAGAGAGAGTATTAAGAGGGAAATACAGAATTCCCTTCTACATGTCTACAGACTGT  
GAAAACCTTCTCAAACGTTTCTGTTGCTAAATCCAATTAAACGCGGCACTCTAGAGCAA  
ATCATGAAGGACAGGTGGATCAATGCAGGGCATGAAGAAGATGAACTCAAACCATTTGTT  
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TCACAAGAAGAAATTCAGAATCTCTTAGTAAGATGAAATACGATGAAATCACAGCTACA  
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AATCTTTCACTTGCTAAGGTTAGGCCGAGCAGTGATCTCAACAACAGTACTGGCCAGTCT  
CCTCACCAAAAGTGCAGAGAAGTGTCTTCAAGCCAAAAGCAAAGACGCTACAGTGAC  
CATGCTGGACCAGCTATTCTTCTGTTGTGGCGTATCCGAAAAGGAGTCAGACAAGCACT  
GCAGATGGTGACCTCAAAGAAGATGGAATTTCTTCCCGGAAATCAAGTGGCAGTGCTGTT  
GGAGGAAAGGGAATTGCTCCAGCCAGTCCCATGCTTGGGAATGCAAGTAATCCTAATAAG  
GCGGATATTCTGAACGCAAGAAAAGCTCCACTGTCCCTAGTAGTAACACAGCATCTGGT  
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ACACACAGTATCAGTAGTGACGCCACCCAGATCGAATCCGCTTCCCAAGAGGCACTGCC  
AGTCGTAGCACTTTCCACGGCCAGCCCCGGGAACGGCGAACCAGCAACATATAATGGCCCT  
CCTGCCTCTCCCAGCCTGTCCCATGAAGCCACACCATTTGTCCCAGACTCGAAGCCGAGGC  
TCCACTAATCTCTTTAGTAAATTAACCTCAAACCTCACAAGGAGTCGCAATGTATCTGCT  
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AAAACCACTAGTTCAATGGATCCCGGGGACATGATGCGGGAAATCCGCAAAGTGTGAGC  
GCCAATAACTGCGACTATGAGCAGAGGGAGCGCTTCTTGCTCTTCTGCGTCCACGGAGAT  
GGGCACGCGGAGAACCTCGTGCAAGTGGGAAATGGAAGTGTGCAAGCTGCCAAGACTGTCT  
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SEQ ID NO: 35\_W90839\_M

AAAGGGCCGTCTGGTCCAGCCGTTCCCTGGGTGCCCGTTGCCGGAACCTCTATCGCTTCC  
TGCCCTGAGGAACAACCCCATGTGGGCAACTATAGGCTGCTAAGGACCATCGGGAAGGGC  
AACTTCGCCAAAGTCAAGCTGGCTCGGCATATCCTCACGGGCCGGGAGGTCGCTATTAAG  
ATCATTGATAAGACCCAGCTGAACCCAGTAGCTTGCAAGCTGTTGAGAGAGTCCGA  
ATTATGAAGGGACTCAACCACCCCAACATCGTGAAGCTTTTGGAGGTGATAGAGACGGAG  
AAGACGCTATACCTGGTGATGGAATACGCTAGCGCAGGAGAAGTGTGTTGACTACCTCGTG  
TCGCACGGCCGCATGAAGGAGAAGGAGGCTCGAGCCAAGTTCCGGCAGATCGTGTCAGCC  
GTGCACTACTGTCATCAGAAGAACATTGTACACAGGGATCTAAAGGCTGAAAACCTGTTG  
CTGGATGCCGAGGCCAACATCAAAATCGCCGACTTCCGGCTTCAGCAATGAGTTCACGCTG  
GGCTCCAAGCTGGACACCTTCTGTGGGAGCCCCCATAACGCCGCCCCAGAGCTGTTCCAG  
GGCAAGAAGTATGATGGGCCAGAGGTGGACATCTGGAGCCTGGGTGTCATCCTGTACACG  
CTGGTCAGCGGCTCCCTGCCCTTCGATGGGCACAACCTCAAGGAGCTGCGGGAGCGAGTC  
CTCAGAGGAAAGTACCGGGTCCCTTCTACATGTCTACAGACTGCGAGAGCATTTCTGCGG

FIGURE 22

AGATTTCTGGTGCTGAACCCCGCAAAACGCTGTACTCTGGAGCAAATCATGAAAGACAAA  
TGGATCAACATCGGCTATGAGGGTGAGGAGCTGAAGCCAGACACGGAGCTCAAAGAAGAG  
CGGATGCCGGGTGCGAAAGCGAGCTGCAGTGCAGTGGGCAGTGGAAGTCGAGGCTTGCCC  
CCCTCCAGCCCCATGGTCAGCAGTGCCACAAACCCCAATAAGGCAGAGATCCCTGAGCGG  
CGGAAGGACAGCACTAGCACCCCTAACAACTCCCCCCCAGCATGATGACCCGAAGAAAC  
ACCTATGTGTGCACAGAGCGACCAGGATCTGAACGCCCCGTCCTTGTTGCCAAATGGCAA  
GAAATAGCTCCGGTACCTCGCGGGTGCCCCCTGCCTCGCCTTCCAGTCATAGCCTGGCT  
CCCCCGTCAGGCGAGCGGAGCCGCTGGCTCGGGGCTCCACCATCCGCAGCACCTTCCAT  
GGGGGCCAGGTCCGAGACCGGCGGGCAGGGAGCGGGAGTGGCGGGGGTGTGCAGAATGGA  
CCCCCAGCCTCACCCACGCTTGCCACAGAGGCCGCACCCCTGCCCTCCGGGCGGCCTCGC  
CCCACCACCAACCTCTTACCAAGCTGACCTCCAACTGACCCGAAGGGTCACAGACGAA  
CCTGAGAGAATCGGGGGACCTGAGGTACAAGTTGCCATCTACCTTGGGATAAAACGGAA  
ACCGCCCCCAGGCTGCTCCGATTCCCCTGGAGTGTGAAGCTGACCAGCTCGCGACCTTCC  
TGAGGCCCTGATGGCTGCCCTGCGACAGGCCACA

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GTAGCCGGCTTGGCGTGACCGTCGCCTGATCCAGTTGTTAGAGGTGGAAGCTTGGCAGTT  
GGCCTCCCTTCTTCCCATGAGAGTTCGGGGGCTTAACAGTCTTTGAAGAGGACCAGAGATG  
CCTTTCCCAGAGCCTCCCTTGCCAGTGTACAGAGGGGCCAGCTGCACAGACCACTGC  
TGAGCCCAGCAGGTGCTTTTCTCAGCCACAGACACCTGAGCAGAAGGAATGGGCTTTC  
CAGACTCTGCCAGAGCAGGACGGCGCTCTCTGAAGACAGATGGAGCTCCTATTGTCTATC  
ATCACTGGCTGCCCAGAATATTTGTACAAGTAACTGCACTGCCCTGCTGCCCTGAGCA  
CACGGACCCGTCCGAACCGCGGGGCGAGTGTGTCTGCTGCTCCCTGCTGCGGGGACTGTC  
CTCAGGGTGGTCTCCTCACCTCTGCTTCCGGCCCCCTGTGTGCAACCCTAACAAAGGCCATCTT  
CACGGTGGATGCCAAGACCACAGAGATCCTCGTTGCTAACGACAAAGCTTGCGGGCTCCT  
GGGGTACAGCAGCCAGGACCTGATTGGCCAGAAGCTCACGCAGTTCTTTCTGAGGTGAGA  
TTCTGATGTGGTGGAGGCCCTCAGCGAGGAGCACATGGAGGCCGACGGCCACGCTGCGGT  
GGTGTGTTGGCACGGTGGTGGACATCATCCCCGTAGTGGGGAGAAGATTCCAGTGTCTGT  
GTGGATGAAGAGGATGCGGCAGGAGCGCCGCTATGCTGCGTGGTGGTCTCTGGAGCCCGT  
GGAGAGGGTCTCGACCTGGGTGCTTTCCAGAGCGATGGCACCATCACGTGATGTGACAG  
TCTCTTTGCTCATCTTCACGGGTACGTGTCTGGGGAGGACGTGGCTGGGCAGCATATCAC  
AGACCTGATCCCTTCTGTGCAGCTCCCTCCTTCTGGCCAGCACATCCCAAAGAATCTCAA  
GATTCAGAGGTCTGTTGGAAGAGCCAGGGACGGTACCACCTTCCCTCTGAGCTTAAAGCT  
GAAATCCCAACCCAGCAGGAGGAGCGACCACCGGTGAGGCGGCCCCCTGTGAGCGGCTA  
CCGGGCATCTGTCTGGGTGTTCTGCACCATCAGTGGCCTCATCACCTCCTGCCGGATGG  
GACCATCCACGGCATCAACCACAGCTTCGCGCTGACACTGTTTGGTTACGGAAAGACGGA  
GCTCCTGGGCAAGAAATACACTTTCCTGATTCCTGGTTTCTACAGCTACATGGACCTTGC  
GTACAACAGCTCATTACAGCTCCCAGACCTGGCCAGCTGCCTGGACGTGCGCAATGAGAG  
TGGGTGTGGGGAGAGAACCTTGGACCCGTGGCAGGGCCAGGACCCAGCTGAGGGGGGCCA  
GGATCCAAGGATTAATGTCGTGCTTGTGTTGGCCACGTTGTGCCCCGAGATGAGATCCG  
GAAGCTGATGGAAGCCAAGACATCTTACCGGGACTCAGACTGAGCTGATTGCTGGAGG  
CCAGCTCCTTTCTGCCTCTCACCTCAGCCTGCTCCAGGGGTGGACAATGTCCCAGAAGG  
AAGCCTGCCAGTGCACGGTGAACAGGCGCTGCCCAAGGACCAGCAAATCACTGCCTTGGG  
GAGAGAGGAACCTGTGGCAATAGAGAGCCCCGGACAGGATCTTCTGGGAGAAAGCAGGTC  
TGAACCAGTGGATGTGAAGCCATTTGCTTCTGCGAAGATTCTGAAGCTCCAGTCCCAGC  
TGAGGATGGGGCAGTGATGCTGGCATGTGTGGCCTGTGTGAGAAGGCCAGCTAGAGCG  
GATGGGAGTCAGTGGTCCCAGCGTTTACAGCCTTTGGGCTGGGGCTGCCGTGGCCAAGCC  
CCAGGCCAAGGGTCAGCTGGCGGGGGGACGCTCCTGATGCACTGCCCTTGCTATGGGAG  
TGAATGGGGCTTGTGGTGGCGAAGCCAGGACTTGGCCCCCAGCCCCCTCTGGGATGGCAGG  
CCTCTCGTTTGGGACACCTACTCTAGATGAGCCGTGGCTGGGAGTGGAAAACGACCGAGA

FIGURE 2AA

AGAGCTGCAGACCTGCTTGATTAAGGAGCAGCTGTCCCAGTTGAGCCTTGACAGGAGCCCT  
GGATGTCCCCACGCCGAACCTCGTTCCGACAGAGTGCCAGGCTGTCACCGCTCCTGTGTG  
GTCCTGCGATCTGGGAGGCAGAGACCTGTGCGGTGGCTGCACGGGCAGCTCCTCAGCCTG  
CTATGCCCTTGGCCACGGACCTCCCTGGGGGCCTGGAAGCAGTGGAGGCCAGGAGGTGA  
TGTGAATTTCGTTTTCTGGAACCTCAAGGAACTCTTTTTCAGTGACCAGACAGACCAAAC  
GTCATCAAATTGTTCTGTGCTACGTCTGAACTCAGAGAGACACCCTCTTCCTTGGCAGT  
GGGCTCCGATCCAGATGTAGGCAGTCTCCAGGAACAGGGGTCTGTGTCTTGGATGACAG  
GGAGCTGTTACTACTGACCGGCACCTGTGTTGACCTTGGCCAAGGCCGACGGTTCCGGGA  
GAGCTGTGTGGGACATGATCCAACAGAACCGCTTGAGGTTTGTGGTGTCTCTGAGCA  
TTATGCAGCAAGCGACAGAGAAAGCCCAGGACACGTTCCCTCCACGTTGGATGCTGGCCC  
TGAGGACACGTGCCCCATCAGCAGAGGAGCCAAGGCTGAACGTCCAGGTACCTCCACGCC  
CGTGATCGTGATGCGCGGGGCTGCTGGCCTGCAGCGGGAGATCCAGGAGGGTGCCTACTC  
CGGAGCTGCTACCATCGAGATGGCTTACGGCTGAGTATACAGTTTGAGGTGAGGCGGGT  
GGAGCTCCAGGGCCCCACACCTCTGTTCTGCTGGCTGGTGAAGACCTCCTCCACAG  
CCAACGCGACTCAGCCGCCAGGACCCGCTGTTCTTCCAGCCTGCCCGGCTCCACCCA  
CTCTACCGCTGCTGAGCTCACCGGACCCAGCCTGGTGAAGTGCTCAGAGCCAGACCCTG  
GTTTGAGGAGCCCCCAAGGCTGTGGAAGTGGAGGGGTTGGCGGCCTGTGAGGGCGAGTA  
CTCCCAAAGTACAGTACCATGAGCCCGCTGGGCAGTGGGGCCTTCGGCTTCGTGTGGAC  
TGCTGTGGACAAGGGAAAAACAAGGAGGTGGTGGTGAAGTTTATTAAGAAGGAGAAGGT  
CTTGAGGATTGTTGGATTGAGGATCCCAAACCTGGGAAAGTTACTTTAGAGATCGCAAT  
TCTATCCAGGGTGGAGCACGCCAATATCATCAAGGTATTGGATATATTTGAAAACCAAGG  
GTTCTTCCAGCTTGTGATGGAGAAGCACGGCTCCGGCCTAGACCTCTTCGCTTTCATCGA  
CCGCCACCCAGGCTGGATGAGCCCCCTGGCGAGCTACATCTTCCGACAAGTGAGAGCAGG  
CCAGAGCCGTCTAGTGTGAGCAGTGGGATACCTGCGCTTGAAGGACATCATCCACCGTGA  
CATCAAGGATGAGAACATCGTGATCGCTGAGGACTTCACAATCAAGCTGATAGACTTTGG  
CTCGGCCGCTACTTGGAAGGGGAAAATTATTTTATACTTTTGTGGGACCATCGAGTA  
CTGTGCACCGGAAGTTCTCATGGGGAATCCCTACAGAGGGCCGGAGCTGGAGATGTGGTC  
TCTGGGAGTCACTCTGTACACGCTGGTCTTTGAGGAGAACCCCTTCTGTGAGCTGGAGGA  
GACCGTGGAGGCTGCCATACACCCGCCATACCTGGTGTCCAAAGAACTCATGAGCCTTGT  
GTCTGGGCTGCTGCAGCCAGTCCCTGAGAGACGCACCACCTTGGAGAAGCTGGTGACAGA  
CCCGTGGGTAAACACAGCCTGTGAATCTTGCTGACTATACATGGGAAGAGGTGTTTCGAGT  
AAACAAGCCAGAAAGTGGAGTTCTGTCCGCTGCGAGCCTGGAGATGGGGAACAGGAGCCT  
GAGTGATGTGGCCAGGCTCAGGAGCTTTGTGGGGGCCCCGTTCCAGGCGAGGCTCCTAA  
TGGCCAAGGCTGTTTGCATCCCGGGGATCCCCGTCTGCTGACCAGCTAAACACCAATTTCT  
TTCCTGCTTTTCTCCACTTGGTTTGGAAAATCACACAGTTTTCAGGCTCCATCTGTTTG

SEQ ID NO: 37\_AA544838\_M 406786\_M

CCACGCGTCCGCATCCCTGCTTGGATGAGCCCCTGGCGAGTTTCATCTTTCGACAACCTAG  
TGTCTGCTGTAGGATACCTGCACTCCCAAGGCATCATCCATAGAGACATCAAGGATGAGA  
ACATTGTGATTGCTGAGGACTTCACAATTAAGCTGATAGATTTTGGCTCAGCTGCCTACT  
TAGAGAGGGGGCAAACCTATTTTATACTTTTGTGGAACAATCGAATACTGTGCACCTGAGG  
TTCTCATTGGAAATCCCTACAGAGGGCCAGAGCTGGAGATGTGGTCTCTGGGGGTACCCC  
TGTACACGCTCATCTTCGAGGAGAATCCCTTCTGTGAGGTGGAGGAGACCATGGAGGCAG  
TTATTCATCCCCATTCCTGGTTTCCCAAGAACTTATGAGTCTTCTGTCTGGACTGCTGC  
AGCCTTGCCCTGAGCAGCGGACCACTTTGGAGAAGCTGATCAGGGACCCCTGGGTGACAC  
AGCCTGTGAACCTTGCTAGCTATACTTGGGAAGAGGTGTGTAGGACCAACCAGCCAGAAA  
GTGGCCTGCTGTGAGCTGCAAGTCTGGAGATTGGGAGTAGGAGTCCAAGTGAAATGGCTC  
AGAGAGAGGGTCTCTGTGGGCCTCCTGCTCCCAGGGAGACTCGTGGTGACCAGCACTGCT  
TGCATCTTAAGGACCCCTCTTTGCCAGTCAGCTGAGCAAGCTCTCCTGCTCTTTGGTTTG  
GGCAGTTGTATGGATTTCAGGGCTTTCTACCTGGAGAAAGGAAGTTGTGAAGGATTGGGA

## FIGURE 2BB

TGACTTCTGCTTCTAGATTCCCTATGCAAATGCTACAAGAGCCTGCGATGCTAGTTTTCTT  
AGGTTTATGATATAGACTTGTAATTCATGTTTTTTTATAACCTTGAAAATCATTCTAATG  
TTCAGTTATACTGTACTATTAAAGGGCTTTAAGTTGTAAGCCTCAGAAAGACACAAGGAG  
TGTTTAAGTTCTCTATTTTTGTGTTTGTGTTTGTGCTTGTAAGTTTTTGAGACAGGATCTC  
ACCATGTAACCTTTGGCTGGCCTGGAACCACTATGTAGACCAGGTAGACCTTAAACTGA  
CAGATCTGCCTGCGCTTGCTCCCAAGCATTAGGACTGATGGTGTGTGTACCATGCCCCA  
GTTCTTCCTGGTTTTGTGTGTAGGTTTTCTTTCCCACTGACTTGGTACATGTGACATGTGA  
CAGATGTATGGAGTCTATAGAAGTGGCCAGACAAAATGGCCAGAATATTTATTTATTTT  
CTTAAAAATTTCCAAATTAAAGCTACTTAGTTAACAGTTAAACTGGCCAGGACTATATG  
AGATAAACTTGGTTTTCTATTTCTTTTGT

SEQ ID NO: 38\_AA785735\_H  
GGCAGGAGGCGCGCTGGCTGGGCCCTGCGGAGGANGGGAAGGAGCGAAGGAGCGAAGGA  
GCAAGCGGAGCGCAGTTCCGCCAAGCCAAGCCGCGCTGCCAACCTCCCGCCCCGCGCG  
CTCCTGTCCGCGGTGTCTAGCAGCGGGGCCAGCATGGTTCATGGCGGATGGCCCGAGGCA  
CTTGACGCGCGGGCCGGTCCGGGTGGGGTCTACGACATCGAGGGCACGCTGGGCAAGGG  
CAACTTCGCTGTGGTGAAGCTGGGGCGGCACCGGATCACCAGACGGAGGTGGCAATAAA  
AATAATCGATAAGTCTCAGCTGGATGCAGTGAACCTTGAGAAAATCTACCGAGAAGTACA  
AATAATGAAAATGTTAGACCACCCTCACATAATCAAACCTTTATCAGGTAATGGAGACCAA  
AAGTATGTTGTACCTTGTGACAGAATATGCCAAAAATGGAGAAATTTTGTACTATCTTGC  
TAATCATGGCCGGTTAAATGAGTCTGAAGCCAGGCGAAAATCTGGCAAATCCTGTCTGC  
TGTTGATTATTGTCTGTCGGAAGATTGTGCACCGTGACCTCAAAGCTGAAAATCTCCT  
GCTGGATAACAACATGAATATCAAATAGCAGATTTTCGGTTTTGGAAATTTCTTTAAAG  
TGGTGAACCTGCTGGCAACATGGTGTGGCAGCCCCCTTATGCAGCCCCAGAAGTCTTTGA  
AGGGCAGCAGTATGAAGGACCACAGCTGGACATCTGGAGTATGGGAGTTGTTCTTTATGT  
CCTTGTCTGTGGAGCTCTGCCCTTTGATGGACCGACTCTTCCAATTTTGAGGCAGAGGGT  
TCTGGAAGGAAGATTCCGGATTCCGTATTTTCATGTGAGAAGATTGCGAGCACCTTATCCG  
AAGGATGTTGGTCTTAGACCCATCCAAACGGCTAACCATAGCCCAAATCAAGGAGCATAA  
ATGGATGCTCATAGAAGTTCCTGTCCAGAGACCTGTTCTCTATCCACAAGAGCAAGAAAA  
TGAGCCATCCATCGGGGAGTTTAAATGAGCAGGTTCTGCGACTGATGCACAGCCTTGGAAT  
AGATCAGCAGAAARCCATTGAGTCTTTGCAGAACAGAGCTATAACCACTTTGCTGCCAT  
TTATTTCTTGTGTTGGTGGAGCGCCTGAAATCACATCGGAGCAGTTTCCCAGTGGAGCAGAG  
ACTTGATGGCCGCCAGCGTCGGCCTAGCACCATTGCTGAGCAAACAGTTGCCAAGGCACA  
GACTGTGGGGCTCCCAGTGACCATGCATTACCGAACATGAGGCTGCTGCGATCTGCCCT  
CCTCCCCCAGGCATCCAACGTGGAGGCCTTTTCATTTCCAGCATCTGGCTGTCTGCTTGA  
AGCTGCATTTCATGGAAGAAGAGTGTGTGGACACTCCAAAGGTCAATGGCTGTCTGCTTGA  
CCCTGTGCCTCCTGTCTGCTGGTGGGAAGGGATGCCAGTCACTGCCAGCAACATGATGGA  
GACCTCCATTGACGAAGGGCTGGAGACAGAAGGAGAGGGCCGAGGAAGACCCCGCTCATGC  
CTTTGAGGCATTTTCAGTCCACACGCGAGCGGCAGAGACGGCACACTCTGTGAGAAGTGAC  
CAATCAACTGGTCTGTGATGCCTGGGGCAGGGAAAATTTCTCCATGAATGACAGCCCCCTC  
CCTTGACAGTGTGGACTCTGAGTATGATATGGGGTCTGTTTCAGAGGGACCTGAACTTTCT  
GGAAGACAACCTTCCCTTAAGGACATCATGTTAGCCAATCAGCCTTCACCCCGATGAC  
ATCTCCCTTCATAAGCCTGAGACCTACCAACCCAGCCATGCAGGCTCTGAGCTCCCAGAA  
ACGAGAGGTCCACAACAGGTCTCCAGTGAGCTTCAGAGAGGGCCGAGAGCATCAGATAC  
CTCCCTCACCCAGGGAATTGTAGCATTTCAGACAACATCTTCAGAATCTGGCTAGAACCAA  
AGGAATTCTAGAGTTGAACAAAGTGCAGTTGTTGTATGAACAAATAGGACCGGAGGCAGA  
CCCTAACCTGGCGCCGGCGGCTCCTCAGCTCCAGGACCTTGCTAGCAGCTGCCCTCAGGA  
AGAAGTTTCTCAGCAGCAGGAAAGCGTCTCCACTCTCCCTGCCAGCGTGCATCCCCAGCT  
GTCCCCACGGCAGAGCCTGGAGACCCAGTACCTGCAGCACAGACTCCAGAAGCCCAGCCT  
TCTGTCAAAGGCCAGAACACCTGTCAGCTTTATTGCAAAGAACCACCGGAGCCTTGA

## FIGURE 2CC

GCAGCAGCTGCAGGAACATAGGCTCCAGCAGAAGCGACTCTTTCTTCAGAAGCAGTCTCA  
ACTGCAGGCCTATTTTAATCAGATGCAGATAGCAGAGAGCTCCTACCCACAGCCAAGTCA  
GCAGCTGCCCCCTTCCCCGCCAGGAGACTCCACCGCCTTCTCAGCAGGCCCCACCGTTTCAG  
CCTGACCCAGCCCCCTGAGCCCCGTCCTGGAGCCTTCCCTCCGAGCAGATGCAATACAGCCC  
TTTCCTCAGCCAGTACCAAGAGATGCAGCTTCAGCCCCCTGCCCTCCACTTCCGGTCCCCG  
GGCTGCTCCTCCTCTGCCCACGCAGCTACAGCAGCAGCAGCCGCCACCGCCACCACCCCC  
TCCACCACCACGACAGCCAGGAGCTGCCCCAGCCCCCTTACAGTTCTCCTATCAGACTTG  
TGAGCTGCCAAGCGCTGCTTCCCCTGCGCCAGACTATCCCACTCCCTGTCAGTATCCTGT  
GGATGGAGCCCAGCAGAGCGACCTAACGGGGCCAGACTGTCCCAGAAGCCCAGGACTGCA  
AGAGGCCCCCTCCAGCTACGACCCACTAGCCCTCTCTGAGCTACCTGGACTCTTTGATTG  
TGAAATGCTAGACGCTGTGGATCCACAACACAACGGGTATGTCCTGGTGAATTAGTCTCA  
GCACAGGAATTGAGGTGGGTGAGGTGAAGGAAGAGTGTATGTTCTATTTTATTCCAGC  
CTTTTAAATTTAAAGCTTATTTTCTTGCCCTCTCCCTAACGGGGAGAAATCGAGCCACCC  
AACTGGAATCAGAGGGTCTGGCTGGGGTGGATGTTGCTTCCTCCTGGTTCTGCCCCACCA  
CAAAGTTTCTGTGGCAAGTGCTGGAACATAGTTGTAGGCTGAGGCAGGAGAATGGCGTG  
AACCCGGGAGGCGGAGCTTGCACTGAGCCAAGATCGTGCCACTGCACTCCAGCCTGGGCG  
ACTGAGCAAGACTCCACCTCAAAAAAAAAAAAAAAAAAGGACAAGAGCAGTATCATCTGCCTC  
TGTTTCTAAACTGGACAAAGAGATTTTCTTAAAGTTTCTATCATCTCCCTTCTGACAGGT  
TCTACAGTGTGGTCTGAAGCACCTGTAATGTCAGAGCCCTTGTCTGGCCCTTGGTGGCAG  
GTGAACGAAAGCAGTGGAGCCTCTCACCTTCCAGTAGCCTCTCACATTCTTATTTTACCA  
TTTTTGTCTTAATTAAGGTAGCTAGCTGATTCTAGAAGACAGCCATCCTACGTGCACCC  
CCACCTTGTGTCCACATCTTCTCCAGGCAGGTTTCAACCTATCAGCAGACTCAGGCACAC  
ACTGGGGCACAGATAGAGAACCAGGCGGCAGCAGTGCTCGCAGACCCACCCAGGGAGAGC  
TGTGATGGGTTCTGCCCAGATACTCTGCTCGCCACCCACAAGGGAGCAATAGCTTATAT  
TTGTACATTAGTTTTACCAAGCACTTTCTCTTCTAACCTCACAACAATTCTATGAAATT  
AGCTGGGGAGATACTGTCCTTATTTTTTACAGCTGAAGAAACCAAAGCTTTGGGAAGTTT  
GTGACTTCTCTGAGATCACAGCTGGTGATAGAAGGAGCTGGGACACGCGCTTGGGTTGAC  
TGGCTTCTGGTTTTGGTTCTCTGGCTTCTAGTGCTGGAAGAAGCCCTCTCTTCCCTTCT  
CTTTCCTCAGTAGCATCTGACTCTTTTTCATAAGCAAACAGCTGTATAAAACAAAGCCCCCA  
TTTTGGTCAAGCACAGGGTGAATGTGATATTGTTCCCACAACCTTATTCTCCACTCAACA  
GCCGCTGGCTTTGGGGAAGAGGCCGCTTTCAGGTGACAGTGCAGCTGTCCAGGTGGCCG  
TGCAGTGAACCAGGCTGAGGGAGACAAAAACCCCGCAGACCCGCTGCCTTTCAGCGTCC  
AGTTAACTGCAGAAGTTTAGGCTCACCTCAAAGATGTCTAGTTTTTCCAAGTTACAATAC  
AGCAGTTTCTTACAGAACACCCCCCTTCTCAATTGCCAAGGGGCCGATCGCACGGCATC  
AGGCCACCACTGCAGGCCAGCAGATTCCACCCAGGAACGGTCATGAACTCAGCCTTTGT  
CTCAACGAGGGGCGTAACATTTCTTACAGTCAAGCCCCATCAACTAGAAGTGCTTATTA  
CTTTTAGGATTAAAAAGTAATAACAGACTTTGACTTAATACTCTGTCTTTTCAGAGGCA  
AAGTGGGTGGGTAGAGGGGAGCTTTAAAAATAGAAGTACAAAACAACATCCTGGAAACAT  
ATGACCCACAGATGGAATAATGTCACATTCCCCAGTGCAGATAATGGGCTGCTGCTGGCTC  
TGTTGGTGTCTGTCTGCAGAAGATTTGCTCAGTCAAGGAAATTCAAGTGGTGAGACCTTTC  
CACCATGGGTGGTAAGAGAAACCTGCCTTCACCAAATCTCTGAAGGGGAAAGAAGTGGA  
GAGAAAGGTTTGCTTCACTTCGGGGACTGCAGTTTGAGAAATAAAAGGGATACAGAGATA  
TCTGCACTTTGTAGAAAGGGCAAGATTATTTGCTTATATCTGAAGGGAGGTGGGTGGTTT  
TGCTGGATGTTTGGTCTGAAAGAGTTACTTTTGATAAAGTTAATCTAATTGTAGTTATAT  
TTTCTGTGTGCTTTTTTTTAAATTAATAAGAAAAAATTTGGTGAGTTCAGTAGCTTTGGTA  
TTATGAGTGCAAATCATAATAGCTCCAATGTGAAAAAAAAAATCAAAGTATAAATTGTCT  
ACTTAATGTTAGAAAATTGCCTAAAATGCAGTGTAATAAATAATCTCTGTACCAAATAGT  
AATTTAAATGGGGTAATTTTCTGCAAGGAAAATGTAAGTTTTTATGTTTTCAACCCCTCT  
TGA



## FIGURE 2DD

SEQ ID NO: 39\_AA207220\_H

GCTGTGGCTCCCCGTCTGGTGCGGGACCTGTGCCCCGCGCTTCAGCCCTCCCCGCAAGC  
CTATTGATTCCCCTGCCGCCCTTGCTCCACCTCCTGCTCGCCATGGAGTCGCTGGTTTTT  
GCGCGGCGCTCCGGCCCCACTCCCTCGGCCGAGAGCTAGCCCGGCCGCTGGCGGAAGGG  
CTGATCAAGTCGCCCAAGCCCCCTAATGAAGAAGCAGGCGGTGAAGCGGCACCACCACAAG  
CACAACTGCGGCACCGCTACGAGTTCCTGGAGACCCTGGGCAAAGGCACCTACGGGAAG  
GTGAAGAAGGCGCGGGAGAGCTCGGGGCGCCTGGTGGCCATCAAGTCAATCCGGAAGGAC  
AAAATCAAAGATGAGCAAGATCTGATGCACATACGGAGGGAGATTGAGATCATGTTCATCA  
CTCAACCACCCTCACATCATTGCCATCCATGAAGTGTGTTGAGAACAGCAGCAAGATCGTG  
ATCGTCATGGAGTATGCCAGCCGGGGCGACCTTTATGACTACATCAGCGAGCGGCAGCAG  
CTCAGTGAGCGCGAAGCTAGGCATTTCTTCCGGCAGATCGTCTCTGCCGTGCACTATTGC  
CATCAGAACAGAGTTGTCCACCAGATCTCAAGCTGGAGAACATCCTCTTGGATGCCAAT  
GGGAATATCAAGATTGCTGACTTCGGCCTCTCCAACCTCTACCATCAAGGCAAGTTCCTG  
CAGACATTCTGTGGGAGCCCCCTCTATGCCTCGCCAGAGATTGTCAATGGGAAGCCCTAC  
ACAGGCCCAGAGGTGGACAGCTGGTCCCTGGGTGTTCTCTCTACATCCTGGTGCATGGC  
ACCATGCCCTTTGATGGGCATGACCATAAGATCCTAGTGAAACAGATCAGCAACGGGGCC  
TACCGGGAGCCACCTAAACCCCTCTGATTGCCTGNNTGGCCTGATCCGGTGGCTGTTGATG  
GTGAACCCACCCGCCGGGCCACCTGGAGGATGTGGCCAGTCACTGGTGGGTCAACTGG  
GGCTACGCCACCCGAGTGGGAGAGCAGGAGGCTCCGCATGAGGGTGGGCACCCTGGCAGT  
GACTCTGCCCCGCGCTCCATGGCTGACTGGCTCCGGCGTTCCTCCCCCCCCCTCCTGGAG  
AATGGGGCCAAGGTGTGCAGCTTCTTCAAGCAGCATGCACCTGGTGGGGGAAGCACCACC  
CCTGGCCTGGAGCGCCAGCATTCGCTCAAGAAGTCCCGCAAGGAGAATGACATGGCCAG  
TCTCTCCACAGTGACACGGCTGATGACACTGCCCATCGCCCTGGCAAGAGCAACCTCAAG  
CTGCCAAAGGGCATTCTCAAGAAGAAGGTGTACGCTCTGCAGAAGGGGTACAGGAGGAC  
CCTCCGGAGCTCAGCCCAATCCCTGCGAGCCAGGGCAGGCTGCCCCCCTGCTCCCCAAG  
AAGGGCATTCTCAAGAAGCCCCGACAGCGGAGTCTGGCTACTACTCCTCTCCCGAGCCC  
AGTGAATCTGGGGAGCTCTTGGACGCAGGCGACGTGTTTGTGAGTGGGGATCCCAAGGAG  
CAGAAGCCTCCGCAAGCTTCAGGGCTGCTCCTCCATCGCAAAGGCATCCTCAAACCTCAAT  
GGCAAGTTCTCCAGACAGCCTTGGAGCTCGCGGCCCCCACCACCTTCGGCTCCCTGGAT  
GAACTCGCCCCACCTCGCCCCCTGGCCCCGGGCCAGCCGACCCTCAGGGGCTGTGAGCGAG  
GACAGCATCCTGTCTCTGAGTCTTTGACCAGCTGGACTTGCCTGAACGGCTCCAGAG  
CCCCCACTGCGGGGCTGTGTGTCTGTGGACAACCTCACGGGGCTTGAGGAGCCCCCTCA  
GAGGGCCCTGGAAGCTGCCTGAGGCGCTGGCGGCAGGATCCTTTGGGGGACAGCTGCTTT  
TCCCTGACAGACTGCCAGGAGGTGACAGCGACCTACCGACAGGCACTGAGGGTCTGCTCA  
AAGCTCACCTGAGTGGAGTAGGCATTGCCCCAGCCCGGTGAGGCTCTCAGATGCAGCTGG  
TTGCACCCCGAGGGGAGATGCCTTCTCCCCACCTCCCAGGACCTGCATCCCAGCTCAGA  
AGGCTGAGAGGGTTTGCAGTGGAGCCCTGAGCAGGGCTGGATATGGGAAGTAGGCAAATG  
AAATGCGCCAAGGGTTCAGTGTCTGTCTTACGCCCTGCTGAACGAAGAGGATACTAAAGA  
GAGGGGAACGGGAATGCCCGGACAGAGTCCACATTGCCTGTTTCTTGTGTACATGGAGG  
GGCCACAGAGA

SEQ ID NO: 40\_AA426580\_H, MAK\_V\_H

ATGCCGGCGGCGGGCGGGGACGGGCTCCTGGGGGAGCCGGCGGCGCCTGGGGGCGGCGGC  
GGCGCGGAGGACGCGGCCAGGCCCCGCGCGGCCTGCGAGGGAAGTTTCTGCTGCCTGG  
GTGAGCGGCGTGCCCCGCGAGCGGCTCCGCGACTTCAGCACCAACAAGCGCGTGGGCAAC  
TACCTCATCGGCAGCAGGAAGCTGGGCGAGGGCTCCTTTGCCAAGGTGCGCGAGGGGCTG  
CACGTGCTGACCGGGGAGAAGGTGGCCATAAAAGTCATTGATAAGAAGAGGCCAAAAAG  
GACACCTATGTACCAAAAAACCTGCGGCGAGAGGGTCAGATCCAGCAGATGATCCGCCAC  
CCCAATATCACTCAGCTCCTTGATATTTTAGAAACGGAAAACAGCTACTACCTGGTCATG  
GAGCTGTGCCCTGGGGGCAACCTGATGCACAAGATCTATGAGAAGAAGCGGCTGGAGGAG



## FIGURE 2EE

TCCGAAGCCCGCAGATACATCCGACAGCTCATCTCTGCCGTAGAGCACCTGCACCGGGCC  
GGGGTGGTCCACAGAGACTTGAAGATAGAGAATTTGCTACTAGATGAAGACAATAATATC  
AAGCTGATTGACTTTGGTTTGAGCAACTGCGCAGGGATCCTGGGTACTCGGATCCGTTC  
AGCACACAGTGTGGCAGCCCTGCCTACGCTGCACCTGAACTGCTCGCCAGGAAGAAATAC  
GGCCCCAAAATCGATGTCTGGTCCATAGGTGTGAACATGTATGCCATGTTGACCGGGACG  
CTGCCTTTACGGTGGAGCCTTTCAGCCTGAGGGCTTTGTACCAGAAGATGGTAGACAAA  
GAAATGAACCCCCCTCCCCACTCAGCTCTCCACAGGTGCCATCAGTTTCCTGCGCTCTCTC  
CTGGAACCGGATCCTGTGAAGAGGCCAAATATTACAGCAGGCACTGGCGAATCGCTGGCTT  
AATGAGAATTACACGGGCAAAGTGCCCTGTAATGTCACCTATCCCAACAGGATTTCTCTG  
GAAGATCTGAGCCCGAGCGTCGTGCTGCACATGACCGAGAAGCTGGGTACAGAACAGC  
GACGTGATCAACACTGTGCTCTCCAACCGCGCCTGCCACATCCTGGCCATCTACTTCCTC  
TTAAACAAGAACTGGAGCGCTATTTGTCAGGGAAATCTGACATCCAGGACAGCCTCTGC  
TACAAGACCCGGCTCTACCAGATAGAAAAGTACAGGGCCCCCAAGGAGTCCTATGAGGCC  
TCTCTGGACACCTGGACACGAGATCTTGAATTCCATGCCGTGCAGGATAAAAAGCCCCAA  
GAACAAGAAAAAGAGGGGATTTTCTTCATCGACCATTCTCCAAGAAGTTGGACAAGAAC  
CTGCCCTCGCACAAACAGCCCTCAGGCTCGCTTATGACACAGATTCAGAACACCAAAGCC  
CTCCTGAAGGACCGGAAGGCCTCCAAGTCCAGCTTCCCCGACAAAGATTCTTTGGCTGC  
CGCAATATTTTCGCAAAACCTCAGATTCCAATTGTGTGGCTTCTTCTTCATGGAGTTC  
ATCCCCGTGCCACCGCCAGGACCCCGAGGATTGTGAAGAAACCGGAGCCCCATCAGCCA  
GGGCCCGGAAGCACTGGCATCCCCACAAGGAAGACCCCTGATGCTGGACATGGTGGCG  
TCCTTCGAGTCTGTGGATCGCGACGACCACGTAGAAGTGCTGTCTCCCTCTCATCACTAC  
AGGATTCTGAACTCCCCGGTCAGCTTGGCTCGCAGAAATTCCAGCGAGAGGACGCTGTCC  
CCGGGTCTGCCATCCGGAAGCATGTGCGCTCTCCATACTCCTTTGCATCCAACCTCTGGTC  
TCTTTTGCTCACGAAGATAAGAACAGCCCCCAAAAGAGGAGGGCCTGTGTTGCCACCT  
CCGGTTCACAGCAATGGCCCCATGCAGCCTCTGGGGAGCCCCAATTGTGTGAAAAGCCGA  
GGCCGGTTCCCTATGATGGGCATCGGACAGATGTTAAGGAAGCGCCATCAGAGTCTGCAG  
CCATCTGCAGATAGGCCCTGGAGGCCAGCCTGCCCCACTGCAGCCCCCTAGCCCCCTGTG  
AACCTTGCCTTTGACATGGCCGATGGGGTCAAGACCCAGTGCTAA

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ATGGACACAAAGCTGAACATGCTGAACGAGAAGGTGGACCAGCTCCTGCACTTCCAAGAA  
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CACAGGCTGGAGGCCTCCCGGGCACCGGGCCCGGGCGGGGCTGATGGGGTTCCCCACATT  
GACACCCAGGCTGGGTGGCCCGAGGTCTTGGAGCTGGTGAGGGCCATGCAGCAGGATGCG  
GCCAGCACGGTGGCAGGCTGGAGGCCCTCTTCAGGATGGTGGCTGCGGTGGACAGGGCC  
ATCGCTTTGGTGGGGGCCACGTTCCAGAAATCAAAGGTGGCGGATTTCTTCATGCAGGGG  
CGTGTGCCCTGGAGGAGAGGCAGCCCAGGTGACAGCCCTGAGGAGTGGGTAAAAGAGGAG  
GAGGTCTGTTTCATGCCTCCAGTTCCCCCAGCTCCGGGGGCAGCAGGACAGAGCCTGCAG  
AAGGATAAGGGGGAGCTGTCTGCCGAGCAGGGGATCTGGGCCACATTGATGACGCTGGTG  
ATCATGGTGACAGCGGCAAATAAAGAGCGAGTGGAAGAAGAGGGAGGAAAACCAAAGCAT  
GTGCTGAGCACCAGTGGGGTGCAGTCTGATGCCAGGGAGCCTGGGGAAGAGAGCCAGAAG  
GCGGACGTGCTGGAGGGGACAGCGGAGAGGCTGCCCCCATCAGAGCGTCAGGGCTGGGA  
GCTGACCCCGCCAGGCAGTGGTCTCACCGGGCCAGGGAGATGGTGTTCCTGGCCAGCC  
CAGGCATTCCCTGGCCACCTGCCCCCTGCCACAAAGGTGGAAGCCAAGGCTCCTGAGACA  
CCCAGCGAGAACCTCAGGACTGGCCTGGAATTGGCTCCAGCACCCGGCAGGGTCAATGTG  
GTCTCCCCGAGCCTGGAGGTTGCACCAGGTGCAGGACAAGGAGCATCGTCCAGCAGGCCT  
GACCCTGAGCCCTTAGAGGAAGGCACGAGGCTGACTCCAGGGCCTGGCCCTCAGTGCCCA  
GGGCCTCCAGGGCTGCCAGCCCAGGCCAGGGCAACCCACAGTGGTGGAGAAACACCTCCA  
AGGGCAGCCCTGCTGAAGGGCGCTGTGGCCCCGGGCTTCTCTCGGAGGGACCTGGTGT  
CCTAGCATCTTCTGCGCCTGCCTAGGGATCTCCATCCACATACAAGAGATGGATACTCCT

FIGURE 2FF

GGGGAGATGCTGATGACAGGCAGGGGAGCCTTGGACCCACCCTCACCACAGAGGCTCCA  
GCAGCTGCCCAGCCAGGCAAGCAGGGCCACCTGGGACCGGGCGCTGCCTCCAAGCCCCT  
GGGACTGAGCCCGGAGAACAGACCCCTGAAGGAGCCAGAGAGCTCTCCCCGCTGCAGGAG  
AGCAGCAGCCCCGGGGGAGTGAAGGCAGAGGAGGAGCAAAGGGCTGGGGCCGAGCCTGGC  
ACGAGACCAAGCTTGGCCAGGAGTGACGACAATGACCACGAGGTTGGGGCCCTGGGCCTG  
CAGCAGGGCAAAGCCAGGGGCGGGAAACCCTGAGCCTGAGCAGGACTGTGCAGCCAGG  
GCTCCGGTGAGAGCTGAAGCAGTAAGGAGGATGCCCCAGGCGCCGAGGCTGGCAGCGTG  
GTTCTGGATGACAGTCCGGCCCCACCAGCTCCTTTTGAACACCGGGTAGTGAGCGTCAAG  
GAGACCTCCATCTCTGCGGGTTACGAGGTGTGCCAGCACGAAGTCTTGGGAGGGGGTTCGG  
TTTGGCCAGGTCCACAGGTGCACAGAGAAGTCCACAGGCCTCCCACTGGCTGCCAAGATC  
ATCAAAGTGAAGAGCGCCAAGGACCGGGAGGACGTGAAGAACGAGATCAACATCATGAAC  
CAGCTCAGCCACGTGAACCTGATCCAGCTCTATGACGCCTTCGAGAGCAAGCACAGCTGC  
ACCTTGTGTCATGGAGTACGTGGACGGGGGTGAGCTCTTCGACCGGATCACAGATGAGAAG  
TACCACCTGACTGAGCTGGATGTGGTCTGTTCACCAGGCAGATCTGTGAGGGTGTGCAT  
TACCTGCACCAGCACTACATCCTGCACCTGGACCTCAAGCCGGAGAACATATTGTGCGTC  
AATCAGACAGGACATCAAATTAAGATCATTGACTTTGGGCTGGCCAGAAGGTACAAGCCT  
CGAGAGAAGCTGAAGGTGAACCTTCGGCCTCCTGAGTTCCTGGCCCCAGAAGTCGTCAAT  
TATGAGTTTGTCTCATTCCCCACAGACATGTGGAGTGTGGGAGTCATCACCTACATGCTA  
CTCAGTGGCTTGTCCCCATTTCTAGGGGAAACAGATGCAGAGACCATGAATTTTCATTGTA  
AACTGTAGCTGGGATTTTGATGCTGACACCTTTGAAGGGCTCTCGGAGGAGGCCAAGGAC  
TTTGTTCCTCGGTTGCTGGTCAAAGAGAAGAGCTGCAGAATGAGTGCCACACAGTGCCTG  
AAACACGAGTGGCTGAATAATTTGCCTGCCAAAGCTTCAAGATCCAAAACCTCGTCTCAA  
TCCCAACTACTGCTGCAGAAATACATAGCTCAAAGAAAATGGAAGAAACATTTCTATGTG  
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GGGGAGATGGCGCTGTTTGAGTGCCTGGTGGCGGGGCCCCACTGACGTGGAGGTGGATTGG  
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CGCAAATGCAAGCTGCTACTTACATCTGTACATGAGGACGACAGTGGCGTCTACACCTGC  
AAGCTCAGCACGGCCAAAGATGAGCTGACCTGCAGTGCCCGGCTGACCGTGCGGCCCTCG  
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CGTTTCGACTGCAAGATCAGTGGCACCCCGCCCCCTGTTGTTACCTGGACTCATTTTGGC  
TGCCCCATGGAGGAGAGTGAGAACTTGCGGCTGCGGCAGGACGGGGGTCTGCACTCACTG  
CACATTGCCCATGTGGGCAGCGAGGACGAGGGGCTCTATGCGGTGAGTGTGTTAACACC  
CATGGCCAGGCCCCTGCTCAGCCCAGCTGTATGTAGAAGAGCCCCGGACAGCCGCCTCA  
GGCCCCAGCTCGAAGCTGGAGAAGATGCCATCCATTCCCGAGGAGCCAGAGCAGGGTGAG  
CTGGAGCGGCTGTCCATTCCCGACTTCTGCGGCCACTGCAGGACCTGGAGGTGGGACTG  
GCCAAGGAGGCCATGCTAGAGTGCCAGGTGACCGGCCCTGCCCTACCCACCATCAGCTGG  
TTCCACAATGGCCACCGCATCCAGAGCAGCGACGACCGGCGCATGACACAGTACAGGGAT  
GTCCATCGCTTGGTGTTCCTGCGGTGGGGCCTCAGCACGCCGGTGTCTACAAGAGCGTC  
ATTGCCAACAAGCTGGGCAAAGCTGCCTGCTATGCCCACCTGTATGTACAGATGTGGTC  
CCAGGCCCTCCAGATGGCGCCCCGAGGTGGTGGCTGTGACGGGGAGGATGGTCACTC  
ACATGGAACCCCCCAGGAGTCTGGACATGGCCATCGACCCGGACTCCCTGACGTACACA  
GTGCAGCACCAGGTGCTGGGCTCGGACCAGTGGACGGCACTGGTCAAGGCCTGCGGGAG  
CCAGGGTGGGCAGCCACAGGGCTGCGTAAGGGGGTCCAGCACATCTTCCGGGTCTCAGC  
ACCACTGTCAAGAGCAGCAGCAAGCCCTCACCCCTTCTGAGCCTGTGCAGCTGCTGGAG  
CACGGCCCAACCCTGGAGGAGGGCCCTGCCATGCTGGACAAACCAGACATCGTGTATGTG  
GTGGAGGGACAGCCTGCCAGCGTCACCGTCACATTCAACCATGTGGAGGGCCAGGTGCTC  
TGGAGGAGCTGCCGAGGGGCCCTCCTAGAGGCACGGGCGGTGTGTACGAGCTGAGCCAG  
CCAGATGATGACCAGTACTGTCTTCGGATCTGCCGGGTGAGCCGCCGGGACATGGGGGCC

## FIGURE 2GG

CTCACCTGCACCGCCCGAAACCGTCACGGCACACAGACCTGCTCGGTACATTGGAGCTG  
GCAGAGGCCCCCTCGTTTGTAGTCCATCATGGAGGACGTGGAGGTGGGGGAACT  
GCTCGCTTTGCGGTGGTGGTTCGAGGGAAAACCACTGCCGACATCATGTGGTACAAGGAC  
GAGGTGCTGCTGACCGAGAGCAGCCATGTGAGCTTCGTGTACGAGGAGAATGAGTGCTCC  
CTGGTGGTGGTCTCAGCACGGGGGCCAGGATGGAGGCGTCTACACCTGCACCGCCAGAAC  
CTGGCGGGTGAGGTCTCCTGCAAAGCAGAGTTGGCTGTGCATTAGCTCAGACAGCTATG  
GAGGTGAGGGGGTTCGGGGAGGATGAGGACCATCGAGGAAGGAGACTCAGCGACTTTTAT  
GACATCCACCAGGAGATCGGCAGGGGTGCTTTCTCCTACTTGCGGCGCATAGTGGAGCGT  
AGCTCCGGCCTGGAGTTTTCGGGCAAGTTTCATCCCCAGCCAGGCCAAGCCAAAGGCATCA  
GCGCGTCGGGAGGCCCCGGCTGCTGGCCAGGCTCCAGCAGACTGTGTCTCTACTTCCAT  
GAGGCCTTCGAGAGGCGCGGGGACTGGTCAATTGTACCGAGCTCTGCACAGAGGAGCTG  
CTGGAGCGAATCGCCAGGAAACCCACCGTGTGTGAGTCTGAGATCCGGGCCTATATGCGG  
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CCTGTGGGTGTTGCTTTCCTCTGTCTGACAGGAATCTCCCCGTTTGTGGGAAAAT  
GACCGGACAACATTGATGAACATCCGAACTACAACGTGGCCTTCGAGGAGACCACATTC  
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AGACCTACCGCAGAAGAGACCCTAGAACATCCTTGGTTCAAACTCAGGCAAAGGGCGCA  
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GAGCGGGTGTGGGTGACCATGCCCAGAAGGCCACCCCCAGTGGGGGGCTCTCATCTCC  
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CAGGACCAGGAGGCTCCCAGCCCAGAGGCCCTCCCCCTCCCAGGCCAGGAGCCCGCAGCT  
GGGGCTAGCCCCAGGCGGGGAGAGCTCCGCAGGGGCAGCTCGGCTGAGAGCGCCCTGCC  
CGGGCCGGGCGCGGGAGCTGGGCGGGGCTGCACAAGGCGGCGTCTGTGGAGCTGCCG  
CAGCGCCGAGCCCCGGCCCCGGGAGCCACCCGCTGGCCCGGGAGGCTGGGTGAGGGC  
GAGTATGCCAGAGGCTGCAGGCCCTGCGCCAGCGGCTGCTGCGGGAGGCCCCGAGGAT  
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CCCCGGATGGCACGAGCTGCCTCCAGCGAGGCAGCGCCCCACCAGCCCCCACTCGAG  
AACC GGCGCTGCAAAGAGCAGCAGCTTCTCCAGGGTGAGGCGGAGCCCCGGGGCCGG  
CACCGCCGAGCGGGGCGCCCCCTCGAGATCCCCGTGGCCAGGCTTGGGGCCCCGTAGGCTA  
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GCTCCGCAGCCCCCGCACCCAGCCTGCCAAGACAAGGCTCCAGAGCCCAGGCCAGAA  
CCAGTCCGAGCCTCCAAGCCTGCACACCCCCCAGGCCCTGCAAACCTAGCGCTGCCC  
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TCGCAGGGCCCTGCCGCGCCGCTTCAGAGCCCAAGCCCCACGCTGCTGTCTTTGCCAGG  
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GAGCCTGGCCTCGTCCGCGCCTCTCGCTGTCACTGTCCCAGCGGCTGCGGCGGACCCCT  
CCCCGCGCAGCGCCACCCGGCCTGGGAGGCCCGCGCGGGGACGGAGAGAGCTCGGAGGGC  
GGGAGCTCGGCGCGGGGCTCCCCGGTGCTGGCGATGCGCAGGCGGCTGAGCTTCACCCTG

## FIGURE 2HH

GAGCGGCTGTCCAGCCGATTGCAGCGCAGTGGCAGCAGCGAGGACTCGGGGGGCGCGTCC  
GGCCGAGCAGCGCCGCTGTTCCGACGGCTTCGAGGGCCACGTCCGAGGGCGAGAGTCTG  
CGGCGCCTTGCCCTTCCGCACAACAGTTGGCCGCCAGGCCGGCGCCACCACGCCTTCC  
GCCGAGTCCCTGGGCTCCGAGGCCAGCGCCACGTGGGCTCCTCAGCCCCAGGGGAAAGC  
CGAAGCCGGCTCCGCTGGGGCTTCTCTCGGCCGCGGAAGGACAAGGGGTATCGCCACCA  
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TTCCCCCAGTCTTCCACATCAAACTCAAGGACCAGGTGCTGCTGGAGGGGGAGGCAGCC  
ACCCTGCTCTGCCTGCCAGCGGCCTGCCCTGCACCGCACATCTCCTGGATGAAAGACAAG  
AAGTCTTGAGGTGAGAGCCCTCAGTGATCATCGTGTCTGCAAAGATGGGCGGCAGCTG  
CTCAGCATCCCCGGGCGGGCAAGCGGCACGCCGTCTCTATGAGTGCTCGGCCACCAAC  
GTACTGGGCAGCATCACCAGCTCCTGTACCGTGGCTGTGGCCGAGTCCCAGGAAAGCTA  
GCTCCTCCAGAGGTAACCCAGACCTACCAGGACACGGCGCTGGTGCTGTGGAAGCCGGGA  
GACAGCCGGGCACCTTGACGTATACGCTGGAGCGGCAGTGAGTGGAGTGGGGAGTCTGTGTGG  
CACCTGTGAGCTCAGGCATCCCCGACTGTTACTACAACGTGACCCACCTGCCAGTTGGC  
GTGACTGTGAGGTTCCGTGTGGCCTGTGCCAACCGTGCTGGGCAGGGGCCCTTCAGCAAC  
TCTTCTGAGAAGGTCTTTGTGAGGGGTACTCAAGATTCTTCAGCTGTGCCATCTGCTGCC  
CACCAAGAGGCCCTGTACCTCAAGGCCAGCCAGGGCCCCGGCCTCCTGACTCTCCTACC  
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CCCCAAACCCCTCCACGAAGACACAGGGGCTGCAGGCTGCCCGGCCAGCGGAGCCCCACC  
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CCTGAGCCTACCAAGGTGACTGTGCAGAGCCTCAGCCCCGCCAAGGAGGTGGTCAGCTCC  
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GCATCTCAGGGAGAACCAAGGAAGGTGGGCATGGCTGGAGAGGAGGAAAAGGAAGGAGCC  
CCAGGTGTGAGGGCAGTAGGCTGGGAGTCAGTGTGGCAAAGCGGGGCGCAGAGGGAGAAG  
CAGTGGCAGGGGCCAGGGCTGGGACATGAGAGAAGGCAGCGAGGGCGCAGAGGGAGAAG  
AGAGGACTCAGGTGGAGGTGGGGTGGGTGAGTGTGAGCATCCCTCAGAGGAGAAATGTG

GAGAGCTGGAGGCCAGCAGTCACTCACACTCGCTCTGTCCTCCTGTCCAGTGGATACAGC  
CCTGGGCGCTCTGCTGGCCCAAGGATGTCCCCACTGCCCTCCATGGCCTTTGGCCTTCT  
TCCCATTCATATTTATTTATTTATTGACTTTTATGAAGTTTCCCCTTCCATCCGATCCCT  
ACTGCCCATGTTGTCTGACCATCCCTCCCAGCCATCCAGCTGTCTGTCTGTCTGCCACA  
AGGAAATAAAAATGGCAAGCAGCAAAAAAA

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GCCACGGACATCTGGGGAGCGGGTGTGCTCACCTACATCATGCTTAGTGGGTACTCCCCA  
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GTACATCCCTGGAGCCGGCCCTCTCTGCAGGACTGCTTGGCCCCACCCATGGCTGCAAGAT  
GCCTACCTGATGAAGCTGCGCCGCCAGACACTCACCTTCACCACCAACCGGCTCAAGGAA  
TTCCTGGGCGAGCAGCGGCGACGTGCGGGCTGAGGCTGCTACCCGTCACAAGGTGCTGCTC  
CGCTCCTACCCTGGCAGCCCCTAGGTGGCACAGACCCGAGCCCCGGCCACGGGCTTCAACT  
TGGGTTCTCACTCGCGCTGCCAAGGGACATTCCAGAGCCCATGCTGAGCTGGACAGGCAG  
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TAGGCTGGAGTGGAATGCTATATCTCAGGGAGAAGCCAGAAGGGGACATGGCTGAAGAGG  
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## FIGURE 2JJ

AAACGCTGCAATGACATGATGAATCTAGGACGTCTGCAGGGCTTTGAGGGCACTCTGACT  
GCTCAGGGGAAGCTACTGCAGCAGGACACATTCTATGTGATCGAGCTGGATGCAGGCATG  
CAGTCCCGGACCAAAGAGAGGCGCGTGTTCCTCTTCGAGCAGATTGTCATCTTCAGTGAA  
CTGCTCAGGAAGGGATCCCTCACCCCTGGCTACATGTTCAAAGGAGCATCAAGATGAAT  
TACTTGGTCCTGGAGGAGAATGTGGACAATGATCCCTGCAAGTTTGCACCTCATGAACAGA  
GAGACTTCTGAGAGGGTTGTTCTGCAAGCCGCCAACGCTGACATCCAGCAGGCCTGGGTG  
CAGGACATCAATCAAGTCTTAGAAACACAGCGAGACTTTTGAATGCACTGCAATCGCCC  
ATTGAGTATCAACGGAAAGAAAGGAGCACAGCTGTGATGAGGTCTCAACCTGCCAGGCTT  
CCCCAAGCCAGCCCCAGGCCCTACTCCTCTGTTCTGCGGGCTCAGAGAAGCCCCCAAAG  
GGCTCCAGCTATAACCCACCTCTGCCTCCCCTGAAGATATCTACCTCCAATGGCAGTCCA  
GGGTTTGAATACCACCAGCCTGGGGACAAGTTCGAAGCCAGCAAGAACGACCTGGGAGGC  
TGCAATGGGACCTCGTCCATGGCCGTGATCAAAGATTACTATGCACTGAAGGAGAATGAA  
ATCTGTGTGAGCCAAGGTGAGGTGGTCCAGGTCCTCGCCGTCAACCAGCAGAACATGTGT  
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AAGAAGAAAGAACAGGCTGCCCACGAGGCTGCCCTGCTTCAGCACCTACAGCACCCCCAG  
TACATCACTCTCCATGACACCTATGAGTCCCCACATCCTACATCCTGATCTTGGAAGTG  
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GTAGCTTTCTATATCCGAGACATCATGGAGGCTCTGCAGTACCTTCACAAGTGCAGGGTT  
GCACATTTGGACATAAAGCCTGAAAACCTGCTCATTGACCTACGGATTCCAGTGCCTCGA  
GTGAAGCTCATTGACTTGGAGGATGCTGTCCAGATCTCGGGTCACTTCCACATTCACCAC  
CTGCTGGGGAACCCTGAGTTTGCTGCCCCAGAAAGTCATTCAAGGCATCCCCGTCTCCCTG  
GGGACAGACATCTGGAGCATCGGGGTTCTGACATATGTCATGCTGAGTGGGGTCTCCCC  
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CCCCATGAATACTTCTGTGGTGTGAGCAATGCTGCCAGAGATTTTCATCAATGTGATCTTA  
CAGGAAGATTTTCGGAGGCGGCCACAGCAGCCACATGCTTGCAGCATCCATGGCTGCAG  
CCCCATAATGGCAGCTACTCTAAGATCCCCCTGGACACCTCCCGCCTAGCATGCTTCATA  
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AACCGGGTGAACCAAGGGACGTAG

SEQ ID NO: 45\_5R72\_8\_2\_H

CGCCGCTGTTTGTCTCGCGCGGCCCGTCCACTGCCCTGCGGTTGCTCTGCGGGCTGAA  
AAGTTTCTCCCGGTGCAGAATTCGGGGCTCAGCGACAGCCTGCGCCGAGTGTGCGCACCT  
GTCGGAGACCCGCCAGTCCGCGGGCCCCGGCTTTGTTCTGTCGGAAGTGTAGTGGTGAGA

## FIGURE 2KK

AAAAC TCCATGTCTGGGCACGCCTGGCTGATCTTCACCTCTTTCTTCTAGGACCTTCCTC  
TGGGCTGTACGTGTGAATATGTGTCTAGTGCATCCTTAACCTGAGGACTTCACCACTTC  
GAAATTACAGTTTTTACCATCAACTACCTTATCCTTTTTTGGCCTGGTTTTCTTCCTCAA  
CAGTGGAAACATTTTTAAAGTTGCTTTTGTGTCAGAGTTAAACAAATGGCTGATAGTGGC  
TTAGATAAAAAATCCACAAAATGCCCCGACTGTTTCATCTGCTTCTCAGAAAGATGTACTT  
TGTGTATGTTCCAGCAAAAACAAGGGTTCCTCCAGTTTTTGGTGGTGGAAATGTACAGACA  
TCAAGCATTGGTAGTGCAGAATCTTTAATTTCACTGGAGAGAAAAAAGAAAAAATATC  
AACAGAGATATAACCTCCAGGAAAGATTTGCCCTCAAGAACCTCAAATGTAGAGAGAAAA  
GCATCTCAGCAACAATGGGGTCGGGGCAACTTTACAGAAGGAAAAGTTCCCTCACATAAGG  
ATTGAGAATGGAGCTGCTATTGAGGAAATCTATACCTTTGGAAGAATATTGGGAAAAGGG  
AGCTTTGGAATAGTCATTGAAGCGACAGACAAGGAAACAGAAACGAAGTGGGCAATTAAA  
AAAGTGAACAAAGAAAAGGCTGGAAGCTCTGCTGTGAAGTTACTTGAACGAGAGGTGAAC  
ATTCTGAAAAGTGTAAAACATGAACACATCATACATCTGGAACAAGTATTTGAAACGCCA  
AAGAAAATGTACCTTGTGATGGAGCTTTGTGAGGATGGAGAACTCAAAGAAATCTGGAT  
AGGAAAGGGCATTCTCAGAGAATGAGACAAGGTGGATCATTCAAAGTCTCGCATCAGCT  
ATAGCATATCTTCACAATAATGATATTGTACATAGAGATCTGAAACTGGAAAATATAATG  
GTTAAAAGCAGTCTTATTGATGATAACAATGAAATAAACTTAAACATAAAGGTGACTGAT  
TTTGGCTTAGCGGTGAAGAAGCAAAGTAGGAGTGAAGCCATGCTGCAGGCCACATGTGGG  
ACTCCTATCTATATGGCCCCCTGAAGTTATCAGTGCCACGACTATAGCCAGCAGTGTGAC  
ATTTGGAGCATAGGAGTCGTAATGTACATGTTATTACGTGGAGAACCACCCTTTTGGCA  
AGCTCAGAAGCGAAGCTTTTTGAGTTAATAAGAAAAGGAGAACTACATTTTGAAAATGCA  
GTCTGGAATTCCATAAGTGAAGTGTGCTAAAAGTGTTTTGAAACAACCTTATGAAAGTAGAT  
CCTGCTCACAGAATCACAGCTAAGGAACTACTAGATAACCAGTGGTTAACAGGCAATAAA  
CTTTCTTCGGTGAGACCAACCAATGTATTAGAGATGATGAAGGAATGGAAAAATAACCCA  
GAAAGTGTGAGGAAAACACAACAGAAGAGAAGAATAAGCCGTCCACTGAAGAAAAGTTG  
AAAAGTTACCAACCCTGGGGAAATGTCCCTGAGACCAATTACACTTCAGATGAAGAGGAG  
GAAAAACAGTCTACTGCTTATGAAAAGCAATTTCCCTGCAACCAGTAAGGACAACCTTGTAT  
ATGTGCAGTTCAAGTTTCACATCTAGCAAACCTCCTTCCAGCTGAAATCAAGGGAGAAATG  
GAGAAAACCCCTGTGACTCCAAGCCAAGGAACAGCAACCAAGTACCCTGCTAAATCCGGC  
GCCCTGTCCAGAACCAAAAAGAACTCTAAGGTTCCCTCCAGTGTGGACAGTACAAAAA  
CAAAGCTGCTCTTGTTAGCACTTTGATGAGGGGGTAGGAGGGGAAGAAGACAGCCCTATG  
CTGAGCTTGTAGCCTTTTAGCTCCACAGAGCCCCGCCATGTGTTTGCACCAGCTTAAAT  
TGAAGCTGCTTATCTCAAAGCAGCATAAGCTGCACATGGCATTAAAGGACAGCCACCAG  
TAGGCTTGGCAGTGGGCTGCAGTGGAAATCAACTCAAGATGTACACGAAGGTTTTTTAGG  
GGGGCAGATACCTTCAATTTAAGGCTGTGGGCACACTTGCTCATTTTTACTTCAAATTCT  
TATGTTTAGGCACAGCTATTTATAGGGGAAAACAAGAGGCCAAATATAGTAATGGAGGTG  
CCAAATAATTATGTGCACTTTGCACTAGAAGACTTTGTTAGAAAATTACTAATAAACTTG  
CCATACGTATTACAGCAGAAGTGCTTCAGTCATTACATGTGTTTCGTGAGATTTTAGGTT  
GCTATAGATTGTTAAGACAGCTTATTTTAAATGTAGAAAATAGGAGATTTTGTAAGTG  
CTTGCCATTAACTTGCTGCTAAATTCCCAATGTATTGATTAAATCAATAAAAAACAGATG  
TTACTC

SEQ ID NO: 46\_SGK309\_H

GGGTCCGCAGCCCCGCCCTCACAGGCCCTCCTCACTCCCCTAGGTAGATGGCCCCCTCAGG  
GCAGGCCCCGGCGGACACCCCTCCCTCTGGCTGGCGGATGCAGTGCCTAGCGGCCGCCCTT  
AAGGACGAAACCAACATGAGTGGGGGAGGGGAGCAGGCCGACATCCTGCCGGCCAACTAC  
GTGGTCAAGGATCGCTGGAAGGTGCTGAAAAAGATCGGGGGCGGGGGCTTTGGTGAGATC  
TACGAGGCCATGGACCTGCTGACCAGGGAGAATGTGGCCCTCAAGGTGGAGTCAGCCAG  
CAGCCCAAGCAGGTCTCAAGATGGAGGTGGCCGTGCTCAAGAAGTTGCAAGGTTCCGGC  
CTCGGGCAGGGGGATGGGAAGGAAGAGATGATGAAGCCAGGGGCTAAGAGAGGGAAGGAC



## FIGURE 2LL

CATGTGTGCAGGTTTCATTGGCTGTGGCAGGAACGAGAAGTTTAACTATGTAGTGATGCAG  
CTCCAGGGCCGGAACCTGGCCGACCTGCGCCGTAGCCAGCCGCGAGGCACCTTCACGCTG  
AGCACCACATTGCGGCTGGGCAAGCAGATCTTGAGTCCATCGAGGCCATCCACTCTGTG  
GGCTTCCTGCACCGTGACATCAAGCCTTCAAACCTTTGCCATGGGCAGGCTGCCCTCCACC  
TACAGGAAGTGCTATATGCTGGACTTCGGGCTGGCCCCGGCAGTACACCAACACCACGGGG  
GATGTGCGGCCCCCTCGGAATGTGGCCGGGTTTCGAGGAACGGTTCGCTATGCCTCAGTC  
AATGCCCACAAGAACCGGGAGATGGGCCGCCACGACGACCTGTGGTCCCTCTTCTACATG  
CTGGTGGAGTTTGCAGTGGGCCAGCTGCCCTGGAGGAAGATCAAGGACAAGGAACAGGTA  
GGGATGATCAAGGAGAAGTATGAGCACCGGATGCTGCTGAAGCACATGCCGTGAGAGTTC  
CACCTCTTCCTGGACCACATTGCCAGCCTCGACTACTTCACCAAGCCCCGACTACCAAGTTG  
ATCATGTGAGTGTGTTGAGAACAGCATGAAGGAGAGGGGCATTGCCGAGAATGAGGCCTTT  
GACTGGGAGAAGGCAGGCACCGATGCCCTCCTGTCCACGAGCACCTCTACCCCCGCCCCCA  
GCAGAACACCCGGCAGACGGCAGCCATGTTTGGGGTGGTCAATGTGACGCCAGTGCCTGG  
GGACCTGCTCCGGGAGAACACCGCGGATGTGCTACAGGGAGAGCACCTGAGTGACCAGGA  
GAATGCACCCCCAATTCTGCCCGGGAGGCCCTCTGAGGGGCTGGGCCACAGTCCCCACCT  
TGTCCCCACCCCGGGGTCCTGAGGCTGAAGTCTGGGAGGAGACAGATGTCAACCGGAA  
CAAACCTCCGATCAACATCGGCAAAGTAACCTGCCGCCAGGGCGAAGGGCGTGGGTGGCCT  
TTTCTCTACCCCCGATTCCCAGCCTTGTGCCCTGCCCTGTTCTCCTAAGCACCTGT  
CCCCCGCAATCTCCTGCTTGCCCGGCCTCTGTTCCGGTCCCCTCCCCGGCACTAGCC  
TCGCTGTGTCTTCCATCATCATCCTCTGTCTCCTTCACACTGAGGAGACCATCCGCC

SEQ ID NO: 47\_AA234451\_H

GGCGCGCCAGATATCACACGTGCCAAGGGGCTGGCTCAGCGGCGGCGGCGGCAGGAGGGG  
GAGCAGGTGCTGGCACAAGAGCAGCGGCTTGGGGGAGCCGGCAGCAGCAGTAACAGCAGC  
AGCAGCCGCCCGCCGCCCGCCAGTAAACGCGGACCGTACCCAGGGGACTACCCAGCCG  
GCCGGCCCTGGAAGCCGCGCTCGGGTCCC GCCGAGTCCGGCGGTGGGGGATGGGCAGGCA  
GTGGCGGTCCCGCCTGCCGAGGGTTAACCCCCGCCGGTCCCGGTCTGAGCTGGACCAGA  
GCCCTCCTCCAGAAACCCCTGCGTCCGCCACGGCCCAGGTTAAATGGAAACCACCCTTGG  
GAACTGGATGCCTGTGTAGCTGTTCTACCATATCAGTGTATTGCAATGAGTGGGGGAGGA  
GAGCAGCTGGATATCCTGAGTGTGGAATCCTAGTGAAAGAAAGATGGAAAGTGTGAGA  
AAGATTGGGGGTGGGGGCTTTGGAGAAATTTACGATGCCTTGGACATGCTCACCAGGGAA  
AATGTTGCACTGAAGGTGGAATCAGCTCAACAACCAAAACAAGTTCTGAAAATGGAAGTT  
GCTGTTTTGAAAAAGCTGCAAGGGAAAGACCATGTTTGTAGATTTATTGGCTGTGGGAGG  
AATGATCGATTCAACTATGTGGTCATGCAGTTGCAGGGTCGGAATCTGGCAGATCTTCGC  
CGTAGCCAGTCCCAGGCACATTACCATTAGTACCACTCTCCGGCTGGGTAGACAGATT  
TTGGAGTCTATTGAAAGCATTCTTCTGTGGGATCTTGNCATCGAGACATCAAACCGTCG  
AACTTCGCTATGGGTCGCTTTCCTAGTACATGTAGGAAATGTTACATGCTTGATTTTGGC  
TTGGCTCGACAATTTACCAATTCCTGTGGTGACGTGAGACCACCTCGAGCTGTGGCAGGT  
TTTCGAGGGACAGTTCGTTATGCATCAATCAACGCACATCGGAACAGGGAAATGGGAAGA  
CATGATGACCTTTGGTCCTTATTCTACATGTTGGTGGAGTTTGTGGTTGGTCAGCTGCCC  
TGGAGAAAAATAAAGGACAAGGAGCAAGTAGGCTCTATTAAGGAGAGATATGACCACAGG  
CTCATGTTGAAACATCTCCCTCCAGAATTCAGCATCTTTCTAGACCATATCTCTTCTTG  
GATTATTTTACAAAACCAAGACTACCAGCTTCTTACATCCGTGTTTGACAATAGCATCAAG  
ACTTTTGGAGTAATTGAGAGTGACCCTTTTGAAGTGGGAGAAGACTGGAAATGATGGCTCC  
CTAACAACCACCACTACTTCTACCAACCCCTCAGTTGCACACTCGCTTGACCCCTGCTGCA  
ATTGGAATTGCCAATGCTACTCCCATCCCTGGAGACTTGCTTCGAGAAAATACAGATGAG  
GTATTTCCAGATGAACAGCTTAGCGATGGAGAAAATGGCATCCCTGTTGGTGTGTACCA  
GATAAATTGCCTGGATCTCTGGGACACCCCGTCCCCAGGAGAAGGATGTTTGGGAAGAG  
ATGGATGCCAACAAAAACAAGATAAAGCTTGAATTTGTAAGGCTGCTACTGAAGAGGAG  
AACAGCCATGGCCAGGCAATGGTCTTCTCAATGCTCCAAGCCTTGGGTCACCAATTCGT



FIGURE 2MM

GTCCGCTCAGAGATTACTCAGCCAGACAGAGATATTCCACTGGTGCGAAAGTTACGTTCC  
ATTCACAGCTTTGAGCTGGAAAAACGTCTGACCCTGGAGCCAAAGCCAGACACTGACAAG  
TTCCTTGAGACCTGGTATAAAATAGTGATTTTTCTTTTTTAAAGCTTCTAAGGTACCATT  
ATTATTGTTGTCATTGTTGTTATTATTATTGTATATTTCTGTTACATAAAGTCTTTCAA  
TAAGAAATCCTTGCAATTTTTGTAACTGAGTCTATTTCAGCTCCAATTTTCATCCATGTT  
TTTAATTATTATTATCCTGATTCTTAATTATTATAAATTCTATAGCATATCCTTTGGCTT  
TGGAAGCTGAGCAGTAAGAGCTGATGACTTCCTAACACTAGGTACAAGTTAAATGAACAT  
TTTTACAGTAACTTTGTTTAGAAAGTAATCTCTTCCACACAACAGTGTAGTGTGGAGAG  
GGCATGATAAAGATGGCATTAGGCAGAGATGAGGGGAATACATAAAGGAGGGGAAAAAGT  
AATTCATACACAAGGGACGGTGAGTTCAATTCACCTTAGTGAAGACCCTCTAGGAGTAAG  
ATACTGTGGGAAAACAGATACCAATAAGTATATCATGCTTGCCCTAGAGAGTTTGAATC  
TACCTAGAGAGAAAGGAAGGTGAACTTGAGAGATCTATATACATAGGTAAAGATTGTAG  
TGCATGGTTTTGAGGCACATTATCCCTACAACAAATTTTGATAACAGAAGAC

SEQ ID NO: 48\_AA435956\_H

ACTTTTACTATATTCTTTGAGATGACTGTTTTTGATTTAGAGGCGAAATCAGCACGTGGT  
GGCTCAAACTCTCTTATGGATAGTGTTTCTTCCCTCCAGCTTTTCATGTTTCACTTTTG  
CGGGGCTGGCGTACATCCACCACCAACACGTCTTTCACAGGGACCTGAAACCTCAGAAC  
TTACTCATCAGTCACCTGGGAGAGCTCAAAGTGGCTGATTTTGGTCTTGCCCGGGCCAAAG  
TCCATTCCCAGCCAGACATACTCTTCAGAAGTCGTGACCCTCTGGTACCGGCCCCCTGAT  
GCTTTGCTGGGAGCCACTGAATATTCTCTGAGCTGGACATATGGGGTGCAGGCTGCATC  
TTTATTGAAATGTTCCAGGGTCAACCTTTGTTTCTGGGGTTTCCAACATCCTTGAACAG  
CTGGAGAAAATCTGGGAGGTGCTGGGAGTCCCTACAGAGGATACTTGGCCGGGAGTCTCC  
AAGCTACCTAACTACAATCCAGAATGGTCCCCTACGCCTCGAAGCCTTCATGTT  
GTCTGGAACAGGCTGGGCAGGGTTCTTGAAGCTGAAGACCTGGCCTCCAGATGCTAAAA  
GGCTTTCCCAGAGACCGCGTCTCCGCCCAGGAAGCACTTGTTTCATGATTATTTAGCGCC  
CTGCCATCTCAGCTGTACCAGCTTCTGATGAGGAGTCTTTGTTTACAGTTTTCAGGAGTG  
AGGCTAAAGCCAGAAATGTGTGACCTTTTGGCCTCCTACCAGAAAGGTCACCACCCAGCC  
CAGTTTAGCAAATGCTGGTGAAAAGAAAGGGCGAGATCACCAGGTTCTTCCAGGGCTGT  
ATTTCTGCAGTTTTCGGTTTTTCATTTGCTTCAGCTTACTAAGAAGCTTCAAATCTAACTCC  
ATACTGAACAAGGGGCTTTATGTCCTCACCTATGACCTGGAATAGTTTAAATATGGTGT  
CAAGGCAATAGTACATAATAGTGGAAGAAAATTCAGTGGAAGGTTATTGCTATTGTCATT  
TGCATAGAATTTAAGTGATTGATTTAAAAAACTGGACATAAACTAAGTCTAAGAAG

SEQ ID NO: 49\_AA626859\_H

AAATGGAGTTGCTGATGGAGTGATCAAAAGCGTATTATGGCAAACACTTCAAGCTCTTAA  
TTTCTGTACATATACATAACTGTATTTCACAGAGATATAAAACCTGAAAATATTCTAATAAC  
TAAGCAAGGAATAATCAAGATTTGTGACTTCGGGTTTGACAAATTCTGATTCCAGGAGA  
TGCCTACACCGATTATGTAGCTACGAGATGGTACCGAGCTCCTGAACTTCTTGTGGGAGA  
TACTCAGTATGGTTCTTCAGTCGATATATGGGCTATTGGTTGTGTTTTTGAGAGCTCCT  
GACAGGCCAGCCACTGTGGCCTGGAAAATCAGATGTGGACCAACTTTATCTGATAATCAG  
AACACTAGGAAAATTAATCCCAAGACATCAATCAATCTTTAAAGTAACGGGTTTTTCCA  
TGGCATCAGTATACCTGAGCCAGAAGACATGGAACTCTTGAGGAAAAGTTCTCAGATGT  
TCATCCTGTGGCTCTGAACTTCATGAAGGGGTGTCTGAAGATGAATCCAGATGACAGATT  
AACCTGTTCCCAACTCCTGGAGAGCTCCTACTTTGATTCTTTTCAAGAGGCCCAAATTA  
AAGAAAAGCACGTAATGAAGGAAGAAACAGAAGACGCCAACAGAATCAACTGTTGCCTCT  
CATACCAGGAAGCCACATCTCCCCCACACCTGATGGAAGAAAACAAGTCTCCAGTTAA  
ATTTGATCACCTTCCAAACATTTAGGAAAATGTTCTTTCAAGTGCAAAGTAATTTAATAT  
GTACACATTTTGTACAAGTGAGATAGGAATTCAGTGTTTCAAATGCAAATGAGCCATA

## FIGURE 2NN

TGAAAATTAAGATGCCTTCTAGAATTGGTTTGCTCTGATCATTGCTGATTCCCTTTCCCCA  
TGCTTTTACAT

SEQ ID NO: 50\_AA061797\_M  
GAAAATAGCCCTGCGGGAAATCCGTATGCTGAAGTTGAAACACCCAAACCTCGTGAACCT  
CATCGAGGTGTTT CAGAAGAAAGAGAAAGATGCATCTAGTTTTTGAGTACTGTGATCACAC  
ACTGTTAAACGAGCTGGAGAGAAACCCAAACGGAGTTTCTGATGGAGTGATTAAAAGTGT  
GCTATGGCAAACCTTCAAGCCCTTAACCTTCTGT CACAAGCACAATTGTATTTCATCGGGA  
TGTAACAACTGAAAACATCCTAATAACCAAGCAAGGGATGATAAAGATTTGTGACTTTGG  
ATTTGCACGAATTCTAATTCAGGAGACGCCTACACAGACTATGTTGCCACCAGGTGGTA  
CCGAGCCCCCGAACTTCTCGTGGGAGACACGAAGTACGGTTCCTCTGTAGACGTGTGGGC  
CGTCGGCTGTGTTTTTGCAGAGCTCCTGACGGGT CAGCCACTCTGGCCGGGAAAATCCGA  
CGTGGACCAGCTTTACCTGATCATCAGGACGTTGGGGAAGCTGATTCCAAGACACCAGTC  
TATCTTTAGGAGTAACCAGTTTTTCCGCGGCATCAGCATACTGAACCAGAGGACATGGA  
GACTCTTGAAGAAAATTCTCAAATGTT CAGCCTGTGGCTTTAAGTTTCATGAAGGGATG  
CCTGAAGATGAATCCTGATGAGAGGCTGACCTGTGCCCAGCTGCTGGACAGTGCCTACTT  
TGAGTCTTTTCAAGAGGATCAAATGAAAAGAAAAGCCCCGAGTGAGGGGAGAAGCCGAAG  
GCGCCAGCAGAATCAACTGCTGCCTCTTATTCCTGGAAGCCACATCTCCCCACACCTGA  
TGGAAGGAAACAAGTCGTCCAGTTAAAGTTCGATCATCTTCCAAACATTTAGGGGACTCA  
TCCTTCCCAGCACATCCTTTTAATATTGTCTACATAGGAATAAGACGGGAATCCTCAGCA  
TCTCAAATACAGTGAGCGACGTGAACACCAGGGCACCTCTAATCACCACGGGCTCCTCCC  
CTGTGCTTTTTCCACGCCAGCTCCATCTCCTAAAACATTCTCTTTAAATGTTGCAGTATC  
AAAATGGCACATCCGAAAGAGATGCTTCCAGTTTCACCAGAGCCGGGCTTCCTCAGGCAA  
TCGGTACTGTGCATCTGTGGACTTATGCTCCGACCTAGGGAAAGATTTCCACGTAGCCGT  
CTCACTTCAGCCGACCAGTGGTGTCTGAAGCAGACCCAGATCTGCTGGCTGCTGTTTGT  
GGAGGGGATGGCCCTGAGCCCTCTCACTGGAGTTTCTTCTCCGTGCAGCCAGGTCTTACT  
TTAGACTACATTTGTGTTATTGTGGCATGGCAATCGTGAAAGGTGGTCTAGGTTTACCCT  
TGACTCCACAGCAGATGCTAGTCTCCTTCTCGTGAGGAGCTGACAAGTCTGCTTCTAAAA  
CGAAGTAGAGAAATTCCAAACGTGACCAGTTAGTGGACAGACTACAAGGAATCGACCAC  
CATACCACAGTAACGCCCCCTGGATCCCTGGCTGCCACCCACTCTAAGGCTATCCTGGTT  
CACCATGGTTTTCTCTTTCTTTTCTTTTCTTTTAAATCTATTTGTACATATGAGAAAGAGG  
AGAGGGGCGAGAGAAACCTCGTGTGTGAAAATCAAAAGACAAGCAGGAGGCCAGCCTAAG  
CTACATAGCAAGGCCTTTTCTCTACACCCATTCTCTAAGGTTGCTTAAACCCAAGTCCCT  
GCTGCTGATTGTATAAACTATGAATAAGTTCTACATATGTAGGACATATTGTTGTCATTG  
TTGAAATATCTAAGGATCTTGGTAGAAGCAGAAGTGTCTAAATATTCTCCACACTGGTG  
AGTATCTTGGCATTTCATTTCTGACCTCATCACAGATGAACACATCAAAGGATGAGTATG  
TATCACTTTGCATCTTAGAATTCTACCTGTTTTAGCTGCGTTAAACCTTGTGAAAGGGCG  
GGGCCATAACTGAACCTGTGGAGTTCTTGCTGTGTGCAGGAAACCTCTGGTTTTGTCT  
CCAGCATGGAAGAAAACAGCTATAGTCACACCTACCTGAAAGTAGAAATTCAAAGTCACT  
GTCCTTGACTACATATGCAGTCCAAGGCCACGCTGGGCTACACTTCTCCAGGCATGAAGG  
TCCGTGTTTGTATCAAGGGGCAGGAAAGGAGAGTCCAAGGTCAAGGCCAGCCGAGGCTGC  
ATAGTGAGTTGAGGCTCTTCAGCAAAAGAAAAGCAAACTAATAGGAGTCGTTGAAGGTAG  
CCACCGGCCATTTCTCTAAATATCATTCTGTGAAAAGGGGGCTTAGTTTAGTTTAGAAT  
GCATTAATGTATGTAGAAGCTGGGCTATTTAGATTATTTGAAATTGTAGCTATTGTTAA  
TTAGCACTTAATAACTAAGTAGCATTATGGTAGTCTAACTATTAGAGTTTACTACAAAG  
AGGTTTTGATTGAATTATATTAACATATAATATGGATTTTAAAAATTTAAGATGTTTAA  
GAAAGCTATATAAGATTAAACATTTTTGTGGCTGTATTTGTGTATATACCTTGGTTG  
TTCTTTAAATTATTTTAAATAAAAGCCAGAAACATT

FIGURE 200

SEQ ID NO: 51\_AA397553\_H  
ATGCCCAATTTCAGAGAGACATGGGGGCAAGAAGGACGGGAGTGGAGGAGCTTCTGGAACCT  
TTGCAGCCGTCATCGGGAGGCGGCAGCTCTAACAGCAGAGAGCGTCACCGCTTGGTATCG  
AAGCACAAGCGGCATAAGTCCAAACACTCCAAAGACATGGGGTTGGTGACCCCCGAAGCA  
GCATCCCTGGGCACAGTTATCAAACCTTTGGTGGAGTATGATGATATCAGCTCTGATTCC  
GACACCTTCTCCGATGACATGGCCTTCAAACCTAGACCGAAGGGAGAACGACGAACGTCGT  
GGATCAGATCGGAGCGACCGCCTGCACAAACATCGTCACCACCAGCACAGGCGTTCCCCGG  
GACTTACTAAAAGCTAAACAGACCGAAAAAGAAAAAGCCAAGAAGTCTCCAGCAAGTCG  
GGATCGATGAAGGACCGGATATCGGGAAGTTCAAAGCGTTCGAATGAGGAGACTGATGAC  
TATGGGAAGGCGCAGGTAGCCAAAAGCAGCAGCAAGGAATCCAGGTCATCCAAGCTCCAC  
AAGGAGAAGACCAGGAAAGAACGGGAGCTGAAGTCTGGGCACAAAGACCGGAGTAAAAGT  
CATCGAAAAAGGGAAACACCCAAAAGTTACAAAACAGTGGACAGCCCCAAAACGGAGATCC  
AGGAGCCCCCACAGGAAGTGGTCTGACAGCTCCAAACAAGATGATAGCCCCCTCGGGAGCT  
TCTTATGGCCAAGATTATGACCTTAGTCCCTCAGCATCTCATACCTCGAGCAATTATGAC  
TCCTACAAGAAAAGTCTTGGAAGTACCTCGAGAAGGCAGTCGGTCAGTCCCCCTTACAAG  
GAGCCTTCGGCCTACCAGTCCAGCACCCGGTCACCGAGCCCCCTACAGTAGGCGACAGAGA  
TCTGTCACTCCCTATAGCAGGAGACGGTCGTCCAGCTACGAAAGAAGTGGCTCTTACAGC  
GGGCGATCGCCAGTCCCTATGGTGAAGGCGGTCCAGCAGCCCTTTCTGAGCAAGCGG  
TCTCTGAGTCGGAGTCCACTCCCCAGTAGGAAATCCATGAAGTCCAGAAGTAGAAGTCTT  
GCATATTCAAGACATTCTCTCTCATAGTAAAAAGAAGAGATCCAGTTTACGCAGTCGT  
CATTCAGTATCTCACCTGTCAAGCTTCCACTTAATTCCAGTCTGGGAGCTGAACTCAGT  
AGGAAAAAGAAGGAAAGAGCAGCTGCTGCTGCTGCAGCAAAGATGGATGGAAAGGAGTCC  
AAGGGTTACCTGTATTTTTGCCTAGAAAAGAGAACAGTTTCACTAGAGGCTAAGGATTCA  
GGTTTGGAGTCTAAAAAGTTACCCAGAAGTGTAATTTGGAAAAATCTGCCCCAGATACT  
GAACTGGTGAATGTAACACATCTAAACACAGAGGTAAAAAATTCTTCAGATACAGGGAAA  
GTAAAGTTGGATGAGAAGTCCGAGAAGCATCTTGTTAAAGATTTGAAAGCACAGGGAACA  
AGAGACTCTAAACCCATAGCACTGAAAGAGGAGATTGTTACTCCAAAGGAGACAGAAACA  
TCAGAAAAGGAGACCCCTCCACCTCTTCCCACAATTGCTTCTCCCCACCCCTCTACCA  
ACTACTACCCCTCCACCTCAGACACCCCTTTGCCACCTTTGCCCTCCAATACCAGCTCTT  
CCACAGCAACCACCTCTGCCTCCTTCTCAGCCAGCATTTAGTCAGGTTTCTGCTTCCAGT  
ACTTCAACTTTGCCCCCTTCTACTCACTCAAAGACATCTGCTGTGCTCTCAGGCAAAT  
TCTCAGCCCCCTGTACAGGTTTCTGTGAAGACTCAAGTATCTGTAACAGCTGCTATTCCA  
CACCTGAAAACTTCAACGTTGCCTCCTTTGCCCTCCACCCCTTATTACCTGGAGGTGAT  
GACATGGATAGTCCAAAAGAACTCTTCCCTTCAAACCTGTGAAGAAAGAGAAGGAACAG  
AGGACACGTCACCTTACTCACAGACCTTCTCTCCCTCCAGAGCTCCCTGGTGGAGATCTG  
TCTCCCCCAGACTCTCCAGAACCAAAGGCAATCACACCACCTCAGCAACCATATAAAAAG  
AGACCAAAAATTTGTTGTCCTCGTTATGGAGAAAGAAGACAAACAGAAAGCGACTGGGGG  
AAACGCTGTGTGGACAAGTTTGACATTATTGGGATTATTGGAGAAGGAACCTATGGCCAA  
GTATATAAAGCCAGGGACAAAGACACAGGAGAACTAGTGGCTCTGAAGAAGGTGAGACTA  
GACAATGAGAAAGAGGGCTTCCCAATCACAGCCATTCTGTGAAATCAAATCCCTTCGTCAG  
TTAATCCACCGAAGTGTGTTAATCATGAAGGAAATTGTACAGATAAACAAGATGCACTG  
GATTTCAAGAAGGACAAAGGTGCCTTTTACCTTGTATTTGAGTATATGGACCATGACTTA  
ATGGGACTGCTAGAATCTGGTTTGGTGCACCTTTCTGAGGACCATATCAAGTCGTTTCATG  
AAACAGCTAATGGAAGGATTGGAATACTGTCAAAAAAGAAATTTCTGCATCGGGATATT  
AAGTGTCTTAACATTTTGTGTAATAACAGTGGGCAAATCAAACCTAGCAGATTTTGGACTT  
GCTCGGCTCTATAACTCTGAAGAGAGTCGCCCTTACACAAACAAAGTCATTACTTTGTGG  
TACCGACCTCCAGAACTACTGCTAGGAGAGGAACGTTACACACCAGCCATAGATGTTTGG  
AGCTGTGGATGTATTCTTGGGGAACATTACAAAGAAGCCTATTTTCAAGCCAATCTG  
GAACTGGCTCAGCTAGAACTGATCAGCCGACTTTGTGGTAGCCCTTGTCCAGCTGTGTGG  
CCTGATGTTATCAAACCTGCCCTACTTCAACACCATGAAACCGAAGAAGCAATATCGAAGG

## FIGURE 2PP

CGTCTACGAGAAGAATTCTCTTTTCATTCTCTCTGACGCACTTGATTTATTGGACCACATG  
CTGACACTAGATCCTAGTAAGCGGTGCACAGCTGAACAGACCCTACAGAGCGACTTCCTT  
AAAGATGTGCAACTCAGCAAAATGGCTCCTCCAGACCTCCCCACTGGCAGGATTGCCAT  
GAGTTGTGGAGTAAGAAAACGGCGACGTGACGACAAAGTGGTGTGTAGTCGAAGAGCCA  
CCTCCATCCAAAACCTTCTCGAAAAGAACTACCTCAGGGACAAGTACTGAGCCTGTGAAG  
AACAGCAGCCCAGCACCACCTCAGCCTGCTCCTGGCAAGGTGGAGTCTGGGGCTGGGGAT  
GCAATAGGCCTTGCTGACATCACACAACAGCTGAATCAAAGTGAATTGGCAGTGTTATTA  
AACCTGCTGCAGAGCCAAACCGACCTGAGCATCCCTCAAATGGCACAGCTGCTTAACATC  
CACTCCAACCCAGAGATGCAGCAGCAGCTGGAAGCCCTGAACCAATCCATCAGTGCCCTG  
ACGGAAGCTACTTCCCAGCAGCAGGACTCAGAGACCATGGCCCCAGAGGAGTCTTTGAAG  
GAAGCACCCCTCTGCCCCAGTGATCCTGCCTTCAGCAGAACAGATGACCCTTGAAGCTTCA  
AGCACACCAGCTGACATGCAGAATATATTGGCAGTTCTCTTGAGTCAGCTGATGAAAACC  
CAAGAGCCAGCAGGCAGTCTGGAGGAAAACAACAGTGACAAGAACAGTGGGCCACAGGGG  
CCCCGAAGAACTCCCAACAATGCCACAGGAGGAGGCAGCAGCATGTCCTCCTCACATTCTT  
CCACCAGAGAAGAGGCCCCCTGAGCCCCCGGACCTCCACCGCCGCCACCTCCACCCCCT  
CTGGTTGAAGGCGATCTTTCCAGCGCCCCCAGGAGTTGAACCCAGCCGTGACAGCCGCC  
TTGCTGCAACTTTTATCCCAGCCTGAAGCAGAGCCTCCTGGCCACCTGCCACATGAGCAC  
CAGGCCTTGAGACCAATGGAGTACTCCACCCGACCCCGTCCAAACAGGACTTATGGAAC  
ACTGATGGGCCTGAAACAGGGTTCACTGCCATTGACACTGATGAACGAAACTCTGGTCCA  
GCCTTGACAGAATCCTTGGTCCAGACCCTGGTGAAGAACAGGACCTTCTCAGGCTCTCTG  
AGCCACCTTGGGGAGTCCAGCAGTTACCAGGGCACAGGGTCAGTGACGTTTCCAGGGGAC  
CAGGACCTCCGTTTTTGCCAGGGTCCCCTTAGCGTTACACCCGGTGGTGGGGCAACCATT  
CTGAAGGCTGAGGGAAGCAGCAATTCTGTGGTACATGCAGAGACCAAATTGCAAACTAT  
GGGGAGCTGGGGCCAGGAACCACTGGGGCCAGCAGCTCAGGAGCAGGCCTTCACTGGGGG  
GGCCAACTCAGTCTTCTGCTTATGGAACCTATCGGGGGCCTACAAGAGTCCCACCA  
AGAGGGGGAAAGAGGGAGAGGAGTTCTTACTAA

SEQ ID NO: 52\_AA789239\_H

TGAAAATGGAGATGTATGAAACCCTTGGAAAAGTGGGAGAGGGAAGTTACGGAACAGTCA  
TGAAATGTAAACATAAGAATACTGGGCAGATAGTGGCCATTAAAGATATTTTATGAGAGAC  
CAGAACAATCTGTCAACAAAATTGCGATGAGAGAAATAAAGTTTCTAAAGCAATTTTCATC  
ACGAAAACCTGGTCAATCTGATTGAAGTTTTTAGACAGAAAAAGAAAATTCAATTTGGTAT  
TTGAATTTATTGACCACACAGTATTAGATGAGTTACAACATTATTGTGATGGACTAGAGA  
GTAAGCGACTTAGAAAATACCTCTTCCAGATCCTTCGAGCAATTGACTATCTTCACAGTA  
ATAATGTAATCATTTCATCGAGATATAAAACCTGAGAATATTTTAGTATCCCAGTCAGGAA  
TTACTAAGCTCTGTGATTTTGGTTTTGACGAACACTAGCAGCTCCTGGGGACATTTATA  
CGGACTATGTGGCCACACGCTGGTATAGAGCTCCCGAATTAGTATTAAAAGATACTTCTT  
ATGGAAAGTATGTGCCTGTGGATATCTGGGCTTTGGGCTGTATGATCATTGAGATGGCCA  
CTGGAAATCCCTATCTTCCTAGTAGTTCTGATTTGGATTTACTCCATAAAATTGTTTTGA  
AAGTGNATTCATGCCAGAACTGAAAGCTAAATTACTGCAGGAAGCAAAAGTCAATTCAT  
TAATAAGCCAAAAGAGAGTTCTAAAGAAAATGAACTCAGGAAAGATGAAAGAAAAACAG  
TTTATACCAATACACTGCTAAGTAGTTCAGTTTTGGGAAAGGAAATAGAAAAAGAGAAAA  
AGCCCAAGGAGATCAAAGTCAGAGTTATTAAAGTCAAAGGAGGAAGAGGAGATATCTCAG  
AACCAAAAAAGAAAGAGTATGAAGGTGGACTTGGTCAACAGGATGCAAATGAAAATGTTT  
ATCCTATGTCTCCAGATACAAAACCTTGTAACCATTTGAACCAACCAACCCCTATCAATCCCA  
GCACTAATGTAATGGCTTGAAAGAAAATCCACATTGCGGAGGTTCTGTGACAATGCCAC  
CCATCAATCTAATAACAGTAATTTGATGGCTGCAAATCTCAGTTCAAATCTCTTTCACC  
CCAGTGTGAGGTTAACTGAAAGAGCAAAAAAGAGACGCACTTCTTCACAATCTATTGGAC  
AAGTTATGCCTAATAGCAGGCAAGAGGATCCAGGTCCTATTCAAAGCCAAATGGAGAAGG  
GTATATTTAATGAGCGAACAGGTACAGTGACCAATGGCAAATGAGAACAAAAGGAAGC

## FIGURE 2QQ

TGAATTTTCCAGATCTGACAGGAAAGAATTCCATTTTCCAGAATTGCCTGTCACAATAC  
AGTCAAAAGATACAAAAGGAATGGAAGTTAAACAGATAAAAATGCTGAAGAGGGAGTCAA  
AGAAAACAGAGTCATCTAAGATACCAACTTTACTTAACGTGGATCAAAATCAAGAAAAAC  
AAGAGTTTATTCCCTTATCTCTGCTGTCTGCCTGCTGTCTTATTTTACAAATATTGCT  
CTCAGCTAACTATCAGGGTGGAGATGGCCATTGCGAGGGGAAGAATTTGAAGAGAAACAG  
GTTTTTTTTCTGGTAGTGTCTTTTCTTTTACATAGTCCAAAAAATACAAGATGACAACTC  
TTCCCGTTTTATTTATCTACAATAGAAGTGTGATGTGAGTTGTTGTTAAGACAGCCATCC  
ATGTGCATGAGCATCATCCAGCTTTTTTTGTTAGCAAAACATTTACTGTTTTCTTTTCCC  
TTTTAAGACTCTGTTGATGTGATAATTTGATTGGAATTATAAAGTCATCTCTTCTCTGC  
CTTGAA

SEQ ID NO: 53\_AA124976\_M  
CTGGCAGATATAGTTTCATGCTTGTTTACAAATTGATCCTGCTGAGAGGACATCATCTACT  
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CTGAGAGCTAAATTATTACAGGAAGCAAAGGTTAATTCATTTATAAAGCCAAAAGAGAAT  
TTTAAAGAAAATGAACCTGTGAGAGATGAGAAGAAATCAGTTTTTACCAACACCCTGCTC  
TATGGAAATCCATCACTTTATGGCAAGGAAGTGGACAGAGACAAAAGGGCCAAGGAGCTC  
AAAGTCAGAGTCATTAAGGCCAAAGGGGGCAAAGGAGATGTCCAGACCAGAAGAAGCCA  
GAGTATGAAGGCCAGCACCGCCAGCAGGGCACAGCTGATGACACACAGCCCTCATCACTG  
GACAAGAAGCCTTCTGTCTTGGAAGTACAAACCCTCTCAATCCCAGTGAGAATTCTGAC  
GGTGTCAAAGAAGACCCACACGCTGGGGTGTATGATAATGCCACCTATCAACCTGACA  
AGCAGTAATTTGTTGGCCGCAAATCTCAGTTCAAACCTTTCCCACCCCAATTCACGGTTA  
ACTGAAAGAACAAAAAGAGACGCACCTTCTTCAAACTATTGGACAGACTTTGTCTAAT  
AGCAGACAAGAGGACACAGGTCCCACACAAGTCCAAACAGAGAAAGGTGCATTTAATGAG  
CGAACAGGTCAGAATGACCAAAATCGAGTGGGAACAAAAGAAAGCTGAATTTTCCCAA  
TGCGACAGGAAAGAATTCCATTTCCCTGAACTGCCATTACAGTGCGAGCGAAGGAGATG  
AAAGGGATGGAAGTTAAACAGATAAAAGTGCTGAAGAGAGAATCAAAGAAAACAGATTCA  
TCTAAAATACCAACTTTACTTAGTATGGACCCAAATCAAGAAAAACAAGAGGGTGGAGAT  
GGCGATTGTGAGGGGAAGAATTTGAAGAGGAACAGATTTTTTTTTTTTCCGATAGTGCTTT  
GTCTTTTAAGTAATCTTAAAATACAAGCTTGACAATTCCTTCCTTTTTTATTTATATAC  
ACTAGAATGTACATAGGTGCTGCTAAGATAGCCACCCATCCCATCTGCATCAACATCAT  
CTATTTTTTTGGTTTTGCTAGCAAAATTTTACAATTTTTCTCTATCTTCAAAAACCTGT  
TATTTTGATGCTGTGATTGAAATTATAAAGTCACCTCCTCTGTCTGCTTCCTTCCTTGC  
CATGATTACTGAGTGGTAGTCACATGATGTGCCCTGCTCGCACTGCTCTCAGACTGCTG  
AGACTCAAACCTCATAAGCCAGGGGTCTCCTGGGAAGCACTGGCCTCTTCAAGTGGATGC  
TCGATGAACCTTCTTATCTGTTGTCTTAGTAACCACTCGTTGCCATCACATGATGAAAGA  
CATTCTATTGTCCCCAGTGAAGCATTTATAGTACTTACATAACATGTTACAGTGATATGA  
TGTTCCCTAGGTTAACTCCTTGAGATGAACTATTTCTGCACTCTCTGACTCCCCTAGT  
CTAATAGTTCCTTCCATTTAGCCAGAAGAATTTCTGAAGAAGCGATGCACAACCTGGGA  
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GTTAACAT

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AGCGCCTCAGGCCAGCTCAAGATAGCTGACTTTGGCCTGGCCCGGGTCTTCTCTCCGGAT  
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TATGGCGCTCGGCAGTATGACCAGGGCGTTGACCTATGGGCTGTGGGCTGCATCATGGGA  
GAGCTGTTGAATGGGTCCCCCTGTTCCCGGGCGAAAACGACATTGAACAACCTGTGCTGT  
GTGCTTCGCATCCTGGGTACCCCGAGTCTCGAGTCTGGCCGGAGATCACAGAGCTGCCT  
GACTACAACAAGATCTCCTTCGAGGAGCAGGCACCAGTGGCCCTGGAGGAGGTGCTGCCT  
GATGCCTCTCCCCAGGCCTTGACCTGCTGGGCCAGTTCCTCCTTACCCTCCACGACAG

## FIGURE 2RR

CGTATTGCAGCCTCCCAGGCCCTTCTGCATCAGTACTTCTTCACAGCGCCTCTGCCTGCC  
CATCCATCCGAGCTGCCAATTCTCAGCGCCCAGGGGGACCTGCACCCAAGGCTCACCCA  
GGGGCCCCCATGTCCACGACTTCCATGTGGATCGACCTATTGAGGAGTCACTGTTGAAC  
CCAGAACTGATTTCGGCCCTTCATCCCAGAGGGGTGAGATGCTGGTCCAGGCCTTCCTGCT  
CGCCCTAGGAGCACCTCTTTCTGATTTGCCCTCCATGGCCTCCCCACGGCTATATATACCA  
CACCTGGTCCTGCTCCTGAGTGTGCTTGAGGGCTGGGCTCTGGGAGGCAGAACCGTGAGA  
TGTTTCATCCCAGCAGAGAAAGAGACTCACGTCTACAGACAAAGCCTCCAGAACTGCTA  
GCTGTGTCCTTCTCAGGGCCACCCCTCAGTGGTGCCACCCGGCCTTAGAGATGATTGTC  
AGGCTCTGTCCCCTCTTCAAGGACATTGGTACTACAGCACCACCTGGTGGAAGCACAGAG  
TATAAGCTGTCTTCATACTGGGGACACAGCTGGGAAGTCAGACATGTTTTAGTTTTGTT  
CCACTGGGTGAGGATTTGAGGTTTCATATAAAAGCCCTGGGTGTTTTCTGTCTAATTGCACC  
TTGTCTGTTGCTGTTAGGGAAAGGACAATGGTGGGCCTTGATTTCAGAGGGGTGAGGTACT  
CAGAAGGGGCCTCCTGTGAAGGCCATTTGGGTCTCAGGCTTCCCATGCTATTACGGGA  
CTTGAGTGCTCATTTGGGAGCGAGGGTCCAGAAGCTGAGGCCAGGGATGGACAGTCCAG  
TTCCCGAAGCCCACTTCCACATGTGCGGTGGGTGAGTCACTGAGCCTGAGGCTGCCTTG  
CAGATGCGGAAGCAGGCATTCTGGAATCCACTCAGTAAATAAATTCAGTGTGACTCAG

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GAACAACAATAACAGAATAAGGAAGAAAATCTCATGATTACCTCAATAAGTACAGAGAAA  
TCTGGTCACACTACTATCCATTTCATGATTACAACCTCTTCAATACTATCGCGGCCGAGGA  
GGGAAGACGGCAGTTTGGCGACATTTCTCGGCCGAAGGGCCATTTGCTTTTGGCGAGATG  
CGGCATTTCCAAAAGAACTCACTGTCCTGATTGGGATAGCAGAGAAAGCTGGGGACATGAA  
AGCTATCGTGGAAGTCACAAGCGGAAGAGAGATCTCATAGTAGCACACAAGAGAACAGG  
CATTGTAAACCACATCACCAGTTTAAAGAATCTGATTGTCAATTATTTAGAAGCAAGGTCC  
TTGAATGAGCGAGATTATCGGGACCGGAGATACGTTGACGAATACAGGAATGACTACTGT  
GAAGGATATGTTCTTAGACATTATCACAGAGACATTGAAAGCGGGTATCGAATCCACTGC  
AGTAAATCTTCAGTCCGCAGCAGGAGAAGCAGTCCTAAAAGGAAGCGCAATAGACACTGT  
TCAAGTCATCAGTCACGTTTCGNATGAAATCGTGAGACACTTTGGGTGAAGGAGCCTTTGGC  
AAAGTTGTAGAGTGCAATTGATCATGGCATGGATGGCATGCATGTAGCAGTGAAAATCGTA  
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CATGGTCATGTTTGTATTGTGTTTGAACACTACTGGGACTTAGTACTTACGATTTTATTAA  
GAAAACAGCTTTCTGCCATTTCAAATTGACCACATCAGGCAGATGGCGTATCAGATCTGC  
CAGTCAATAAATTTTTTACATCATAATAAATTAACCCATACAGATCTGAAGCCTGAAAAT  
ATTTTGTGTTGTGAAGTCTGACTATGTAGTCAAATATAATTCTAAAATGAAACGTGATGAA  
CGCACACTGAAAAACACAGATATCAAAGTTGTTGACTTTGGAAGTGCAACGTATGATGAT  
GAACATCACAGTACTTTGGTGTCTACCCGGCACTACAGAGCTCCCGAGGTCAATTTGGCT  
TTAGGTTGGTCTCAGCCTTGTGATGTTTGGAGCATAGGTTGCATTCTTATTGAATATTAC  
CTTGGTTTCACAGTCTTTCAGACTCATGATAGTAAAGAGCACCTGGCAATGATGGAACGA  
ATATTAGGACCCATACCACAACACATGATTTCAGAAAACAAGAAAACGCAAGTATTTTCAC  
CATAACCAGCTAGATTGGGATGAACACAGTTCTGCTGGTAGATATGTTAGGAGACGCTGC  
AAACCGTTGAAGGAATTTATGCTTTGTGATGATGAAGAACATGAGAACTGTTTGACCTG  
GTTGGAAGAATGTTAGAATATGATCCAACTCAAAGAATTACCTTGGATGAAGCATTGCAG  
CATCCTTTCTTTGACTTATTAAAAAAGAAATGAAATGGGAATCAGTGGTCTTACTATATA  
CTTCTCTAGAAGAGATTACTTAAGACTGTGTGAGTCAACTAAACATTCTAATATTTTTGT  
AAACATTAAATTTTGTACAGTTAAGTGTAAATATTGTATGTTTTGTATCAATAGCAT  
AATTAACCTGTTAAGCAAGTATGGTCTTGATAATGCATTAGAAAAATTAAATTTT  
TCTTTTTGAAATTACCATTTTTTAAATACCTTTGAAATATCCTTTGTGTCCAGTGATAAT  
GTGATTGATCTTGCCTTTTGTACATGGAGGTACCTCTGAAGTGATTTTTTTTGTAGTAAA  
AGGAAATCTTGACTACTTTATATTCTTAAAGGAATATTCTTTATATACTTCAAATTTAGA

## FIGURE 2SS

ACTTAACTTTAAAAGTTTTCTTCTGTAATTGTTGAACGGGTGATTATTATTAAGTCTAG  
ATAAGCAGGTACTAGAAAACCAAACTCAGAAAATGTTTACTGTTAGAATTCTATTAAATT  
TTAAGTGTTGTATTCTTTTTTCATTGGGTGATGTCAGGGTGATAACCAGACATTCATGGAA  
AGGCATGCAGTTTGTCCATTGTGACAGTTTGTTTAATAAAAACCACATACACACTTTATTT  
AAGATTAAAATCTAACTGGAAAGTCAGCTTGGAAAATGGACATTTCCAAGTATGTTTGGT  
GAGTCACAGATATAAAAATAGAAATTCGTATGAGAGGTTTCAGTTTTTAATACCAAGTCC  
TTAGGAGTCTTAACATTGGCCAGCATCTGTTTATCAAATGACATAAATACGTAAACCTAT  
AAGAATTAAGTTTATTAATTAGGCAATTTATGTCTGTGATAATTCTTACGGGAGAAAGAG  
GATTTGATTGGAAAGCAGTTTGGGAAGAAAGTGCTGCTGAAATTTCCAGAATTTAATTGA  
TTGGTTACATAAACTTTTTGACTTCAAT

SEQ ID NO: 56\_AA557536\_H

AGTAAGGCCCCGCGGCGTCCTGGCCGCCATGTGCACCGTAGTGGACCCTCGCATTGTCC  
GGAGATACCTACTCAGGCGGCAGCTCGGGCAGGGGAGAACATTCCGGGAAATCACGCTCC  
TCCAGGTGAGTGGCCTGGGCCCTCCAGTCCAATCCCCTTGCCCAGGTACAGATCTCTCCA  
GACAGGAGAGAACTGGCCTTCTTGGGCCCCAGAGCACAGCCCCCTCCTGGCCTTCCAGCC  
GCCTCCGACTCTCTCCCCAGGAGTTTGGGGACCATCCCAACATCATCAGCCTCCTTGACG  
TGATCCGGGCAGAGAACGACAGGGACATTTACCTGGTGTGTGAGTTTATGGACACTGACC  
TGAACGCAGTCATCCGGAAGGGCGGCCTGCTGCAGGACGTCCACGTGCGCTCCATCTTCT  
ACCAGCTCCTGCGGGCCACCCGGTTCCCTCCACTCGGGGCACGTTGTGCACCGGGACCAGA  
AGCCGTCCAATGTGCTCCTGGATGCCAACTGCACAGTGAAGCTGTGTGACTTTGGCCTGG  
CCCGCTCCCTGGGCGACCTCCCTGAGGGGCTGAGGACCAGGCCGTGACAGAGTACGTGG  
CCACACGCTGGTACCGAGCACCGGAGGTGCTGCTCTCTTCGCACCGCTACACCGCTTCCCT  
GCCCCAGATACACCTTGGGGTGGACATGTGGAGTCTGGGCTGTATCCTGGGGGAGATGC  
TGCGGGGGAGACCCCTGTTCCCCGGCACGTCCACCCTCCACCAGCTGGAGCTGATCCTGG  
AGACCATCCACCGCCATCTGAGGAGXXXAGGCCACGACAGACGCTGGATGCCCTCCTAC  
CGCCAGACACCTCCCCAGAGGCTTGGACCTCCTTAGGCGACTCCTGGTGTTCGCCCCGG  
ACAAGCGTTAAGCGCGACCCAGGCACTGCAGCACCCCTACGTGCAGAGGTTCCACTGCC  
CCAGCGACGAGTGGGCACGAGAGGCAGATGTGCGGCCCCGGGCACACGAAGGGGTCCAGC  
TCTCTGTGCTGAGTACCGCAGCCGCTCTATCAGATGATCCTGGAGTGTGGAGGCAGCA  
GCGGCACCTCGAGAGAGAAGGGCCCGGAGGTTGTCTCCCCAAGCCAGGCACACCTGCACA  
AACCCAGAGCCGACCCCTCAGCTGCCTTCTAGGACACCTGTGACAGGTCCCAGACCCAGGC  
CCCAGAGCAGCCCAGGCCATGACCCTGCCGAGCACGAGTCCCCCGTGCAGCCAAGAAGC  
TTCCAGGCAGAACTCCGCTCCCCCTGCTCCAACTGCTCTCCTAGGGAATGGGGAAAGGC  
CCCCTGGGGCGAAGGAAGCGCCCCCTTGACACTCTCGCTGGTGAAGCCAAGCGGGAGGG  
GAGCTGCGCCCTCCCTGACCTCCCAGGCTGCGGCTCAGGTGGCCAACCAGGCCCTGATCC  
GGGGTGACTGGAACCGGGGCGGTGGGGTGAGGGTGGCCAGCGTACAACAGGTCCCTCCCC  
GGCTTCCCTCCGGAGGCCCGGCCCGGCGGAGGATGTTTCAGCACCTCTGCCTTGACGGGTG  
CCCAGGGGGGTGCCAGGGCTTTGCTTGGAGGCTACTCCCAAGCCTACGGGACTGTCTGCC  
ACTCGGCACTGGGCCACCTGCCCTGCTGGAGGGGCACCATGTGTGAGCCGCCCTACTCC  
CTTACCTGGCCCTCTGTTCTGCCCCAGCNCCTTCCCAGACCCCTCTCCAGTCTCCTG  
CACCCCTTAGCCCTCCCTGCTTTGCCTGGCCCGTTGAAGTTCCAGGGAGCTTGCCCGGGT  
CTCCTCGGGGAGCAGATGAGGGCCCTGCCC

SEQ ID NO: 57\_N28606\_H, MOK\_H

ATGAAGAACTATAAAGCAATTGGCAAAATAGGAGAGGGAACGTTTTCTGAAGTTATGAAG  
ATGCAAAGCCTGAGAGATGGAACTACTATGCATGTAAACAAATGAAGCAGCGCTTTGAA  
AGTATTGAGCAAGTCAACAACCTACGAGAGATCCAAGCACTGAGGCGCCTGAATCCGCAC  
CCAAACATTCTTATGTTGCATGAAGTGGTTTTTGACAGAAAATCTGGTTCTCTTGCACTA  
ATATGTGAACCTTATGGACATGAATATTTATGAGCTAATACGAGGGAGAAGATACCCATTA



## FIGURE 2TT

TCAGAAAAAAAAATTATGCACTATATGTACCAGTTATGTAAGTCCCTGGATCATATTCAC  
AGAAATGGAATATTTACAGAGATGTAAAACCAGAAAATATACTAATAAAGCAGGATGTC  
CTGAAATTAGGGGACTTTGGCTCCTGCCGGAGTGTCTATTCCAAGCAGCCGTACACGGAA  
TACATCTCCACCCGCTGGTACCGGGCCCCGGAGTGTCTCTCACTGATGGGTCTACACG  
TACAAGATGGACCTGTGGAGCGCCGGCTGTGTGTTCTACGAGATCGCCAGTCTGCAGCCC  
CTCTTTCTGGAGTAAATGAACTGGACCAAATCTCAAAAATCCACGATGTATCGGCACA  
CCCGCTCAGAAGATCCTCACCAAGTTCAAACAGTCGAGAGCTATGAATTTTGATTTTCCT  
TTTAAAAAGGGATCAGGAATACCTCTACTAACAACCAATTTGTCCCCACAATGCCTCTCC  
CTCCTGCACGCAATGGTGGCCTATGATCCCGATGAGAGAATCGCCGCCACCAGGCCCTG  
CAGCACCCCTACTTCCAAGAACAGAGGAAAACAGAGAAGCGGGCTCTGGGCAGCCACAGA  
AAAGCTGGCTTTCCGGAGCACCTGTGGCACCGGAACCACTCAGTAACAGCTGCCAGATT  
TCCAAGGAGGGCAGAAAGCAGAAACAGTCCCTAAAGCAAGAGGAGGACCGTCCCAAGAGA  
CGAGGACCGGCCTATGTCATGGAACCTGCCAAACTAAAGCTTTCGGGAGTGGTCAGACTG  
TCGTCTTACTCCAGCCCCACGCTGCAGTCCGTGCTTGGATCTGGAACAAATGGAAGAGTG  
CCGGTGCTGAGACCCTTGAAGTGCATCCCTGCGAGCAAGAAGACAGATCCGCAGAAGGAC  
CTTAAGCCTGCCCCGCAGCAGTGTGCGCTGCCACCATAGTGCGGAAAGGCGGAAGATAA

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ATGAATAGATACACAACAATCAGGCAGCTCGGGGATGGAACCTACGGTTCCGTCTCTGCTG  
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AATGTAGTCAAATTAAGAAGTTATCAGGGAAAATGATCATCTTTATTTTATCTTCGAG  
TACATGAAGGAAAATCTTTACCAGCTCATTAAGAGAGAGAAATAAGTTGTTTCTGAGTCT  
GCTATAAGGAATATCATGTATCAGATATTACAAGGACTCGCATTTATTACAAACTCGGC  
TTCTTTTCATCGAGACTTAAGCCTGAGAACCTCTCTGCATGGGACCAGAACTTGTGAAA  
ATTGCAGACTTTGGTTTGGCCCCGAGAAATACGATCAAAACCTCCATATACAGATTATGTA  
TCTACCAGATGGTACAGGGCTCCAGAAGTACTCTGAGGTCTACCAACTACAGCTCCCCC  
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CCTGGAGCCAGTGAAATTGACACAATATTCAAAATTTGCCAAGTGCTGGGGACACCAAAA  
AAGACTGACTGGCCTGAAGGCTATCAACTTTCAAGTGCAATGAACTTCCGTGGCCACAG  
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CTGAGAGACATGCTTCAGTGGGATCCCAAGAAACGACCAACAGCTAGTCAGGCACCTCGA  
TATCCTTACTTCCAAGTTGGACACCCACTAGGCAGCACCCACACAAAACCTTCAGGATTCA  
GAAAAACCACAGAAAGGCATCCTGGAAAGGGCAGGCCACCTCCTTATATTAAGCCAGTC  
CCACCTGCCCAGCCACCAGCCAAGCCACACACAGCAATTTCTTCACGACAGCATCAAGCC  
AGCCAGCCCCCTCTGCATCTCACGTACCCCTACAAAGCAGAGGTCTCCAGGACAGATCAC  
CCAAGCCATCTCCAGGAGGACAAGCCAAGCCCGTTGCTTTTCCCATCCCTCCACAACAAG  
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AGTAGGAGAAGGTGGGGTCTTATTTCCAGGTCAACAAAGGATTTCAGATGATTGGGCTGAC  
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AAAAAGAAATCGGTTCTGCTATGCAGAGGGTACACCTAGCACCTATTCCAGACCCTTCC  
CCTGGTTATTCTCCCTGAAGGCCATGAGACCTCATCCTGGGCGACCATTCTTGGACACC  
CAGCCTAGAAGCACTCCTGGGTTGATACCACGGCCTCCAGCCGCCAGCCAGTGCATGGC  
CGGACAGACTGGGCTTCCAAGTACCCATCCCGGCGGTGA



FIGURE 2UU

SEQ ID NO: 59\_AA839940\_M

AGCAGCAACAATGGTGGCATGAGTGCAGAGGAGGAGATAGGGCCTGGGGCTGAGCCTATG  
AGAGGACCAAGCTTGGCTACAAGGGAAGTGGAGAGATGAGACTGTTGGGACCACAGACCTG  
CAGCAAGGCATAGACCCAGGAGCAGTGAGCCCTGAGCCTGGGAAGGACCACGCAGCCAG  
GGCCCAGGAAGAACTGAAGCTGGAAGGGTATCTTCTGCTGCAGAGGCTGCCATTGTGGTT  
CTAGATGACAGCGCAGCACCCCCAGCCCCTTTTGAACACCGGGTAGTGAGCATCAAAGAT  
ACCCTGATCTCAGCAGGCTACACGGTATCCCAACATGAAGTCTTAGGAGGGGGTTCGGTTT  
GGCCAGGTGCACAGGTGTACAGAGAGGTCTACAGGCCTTGCACTGGCAGCCAAGATCATC  
AAAGTGAAGAACGTAAAGGACCGGGAGGATGTGAAGAATGAGGTCAACATCATGAACCAG  
CTCAGCCACGTAAACTTGATCCAACCTTTATGATGCGTTTGAGAGCAAGAACAGCTTCACT  
CTGATCATGGAGTATGTGGATGGAGGCGAACTCTTTGACCGGATCACGGATGAGAAGTAC  
CACCTCACTGAGTTGGATGTGGTCTTGTTACAGAGGCAGATCTGTGAGGGTGTGCATTAC  
CTGCATCAGCACTATATCCTGCACCTGGACCTCAAGCCTGAGAACATATTGTGTGTGAGC  
CAGACAGGGCATCAAATTAAGATCATTGACTTTGGGCTGGCTAGAAGATACAAGCCTCGG  
GAGAAGCTAAAGGTGAACCTTTGGTACTCCGGAGTTCCTGGCCCCAGAAAGTTGTTAACTAT  
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GTTTCCCCGTTACTGGTCAAAGAGAAGAGCTGTAGGATGAGCGCCACACAGTGCCTGAAA  
CACGAGTGGTTAAATCACCTGCCTGCCAAAGCCTCGGGCTCCAACGTTCCGCTCAGATCC  
CAACAACCTGCTGCAGAAATATATGGCTCAGAGTAAATGGAAGAAACATTTCCACGTGGTG  
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CACTGGGCCTGGGAATTTCTGAGGCAACACGAAGTGGTAATATGAAGAGATTACTCAAGA  
TTTTATGTAGATTGGCGCTTTGCTATTATTGATTTTTCTTATTTTGCAAAGAATGATGGA  
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GGAAACAGGCTACGTTGTTGCTCTTCTGTAGGTGAAAGTGTTTTTATTAAAAGCCCTAG  
GAATGTTTTCTGCCTCGTAAGGTCAGCAGGTCTCATATGCTGCTTGCTACCCCGCAGCC  
TTCCTTTTGGTAATAAGAGCAGGCACGCTCAGGATGGGCAGGGAAATCCTACTTGGCTTT  
TGGTCAAATTTGAATTCTAACTTGTGATGATTAAAGAAGCCAGTAGGGAGGGAGGTATG  
GAAGAGGGAGGAATTAGGTCCAACAGTGGGGATGAATTTGACCGAAACATTGTATAAAA  
TTCTTAAAGAATTAATAAAATATATTTTTTAAAGGAG

SEQ ID NO: 60\_AA460132\_H

GGAACCTCAGGCTTCAGAGAGCCGAAAAGTTGGGAGGCGTAACCACTTACAGGCCGGAAG  
TGTCCGGGGTGGACGCATTTCGGGTAGCCGAAGAAGTCCCAGGATTGCCGAAGAAGTCCCA  
GGATTTCCGAAGCGAGCCGAAGCATCGCGACAGTTTTTCAGAGACAGCTGATCGGTTGGAG  
CTGTTGCGCCGAGCAGTCATGGCGGCGGCCAGAGCTACTACGCCGGCCGATGGCGAGGAG  
CCCCCCCCGGAGGCTGAGGCTCTGGCCGCAGCCCGGGAGCGGAGCAGCCGCTTCTTGAGC  
GGCCTGGAGCTGGTGAAGCAGGGTGGCGAGGCGCGGTGTTCCGTGGCCGCTTCCAGGGC  
CGCGCGGCGGTGATCAAGCACCGCTTCCCCAAGGGCTACCGGCACCCGGCGCTGGAGGCG  
CGGCTTGGCAGACGGCGGACGGTGACAGGAGGCCCGGGCGCTCCTCCGCTGTCGCCGCGCT  
GGAATATCTGCCCCAGTTGTCTTTTTTGTGGACTATGCTTCCAACCTGCTTATATATGGAA  
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GATGAAGACCTCATTTCATGGTGATCTCACCACCTCCAACATGCTCCTGAAACCCCCCTG  
GAACAGCTGAACATTGTGCTCATAGACTTTGGGCTGAGTTTCATTTTCAGCACTTCCAGAG  
GATAAGGGAGTAGACCTCTATGTCCTGGAGAAGGCCTTCCTCAGTACCCATCCCAACACT  
GAACTGTGTTTGAAGCCTTTCTGAAGAGCTACTCCACCTCCTCCAAAAAGGCCAGGCCA  
GTGCTAAAAAAATTAGATGAAGTGCGCCTGAGAGGAAGAAAGAGGTCCATGGTTGGGTAG  
AAGAATGTGTATGACAACCACACACAGTGAAGCTCTTTTTTCAAAGTAAATTTGAAGAAA

## FIGURE 2VV

TGCTACAAGTATGAGATGAGATCTAAGTAAAGGTGTTAAGATATTTTTAAGTGGTATGTG  
ATCGTGTCATTATCATCTGCACTTCACTCAAGAGCTTACTATGTGTCTAAGTCATGTTCT  
AGGCAGAATTGGGTATTTAAAGTAAATTGAGGACAGGCTTCTCCCAGATTGTGACATGTA  
TATCTCAGATACATGGGTGTGGCATTGAACCACATAATGAGAACATTATTCTCTTTTTAG  
TCCTTGTGAGACAAGGATGAAGTCTCAGTTGCTGATACTCGCTGAGCTTACTGGCCCTCT  
AACCCAGTGTTTTTTTTTTGTTGTTGTTGTGTACATGTTATATTTATTTTGAACCAGTTT  
AATGGGATACAACCAGCATTTTAAAAAATGAAATAGAATACAGCATGG

SEQ ID NO: 61\_SGK034\_H

CAGAGAGAGAAGGTAAACCAAGGGAACATGCCAGGGCTTCAGAGCACCTTCCTAGCCATG  
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TTCGCGGCGCACGAGGAGAAGATCCAGACCGTGTTTCGAGCAGCTGGTGCTGGTGGACCAC  
CCGAACATCGTGAAGTTGCACAAGTACTGGCTGGATACCTCTGAGGCCCTGCGCGAGGGTC  
ATCTTCATCACAGAGTACGTGTCATCAGGCAGCCTCAAGCAATTCTCAAAAAGACCAAG  
AAGAACCACAAGGCCATGAACGCCCCGGGCTGGAAGCGCTGGTGCACGCAGATCCTGTCT  
GCGCTCAGCTTCCTGCACGCCTGCAGCCCCCAATCATCCACGGGAACCTGACCAGCGAC  
ACCATCTTCATTTCAGCACAAACGGCCTCATCAAGATCGGCTCCGTGTGGCACCGAATCTTC  
TCCAATGCACTTCAGATGATCTCCGAAGCCCCATCCGCGCTGAGCGAGAGGAACCTTCGG  
AACCTGCACTTCTTCCCCCAGAGTATGGAGAGGTGGCCGATGGGACCGCTGTGGACATC  
TTCTCCTTTGGGATGTGTGCGCTGGAGATGGCTGTACTGGAAATCCAGACCAATGGGGAC  
ACCCGGGTACAGAGGAGGCCATTGCTCGCGCCAGGCACTCGCTGAGTGACCCCAACATG  
CGGGAGTTCATCCTTTGCTGCCTGGCCCCGGGACCCTGCCCGCCGGCCCTCTGCCCACAGC  
CTCCTCTTCCACCGCGTGCTCTTCGAGGTGCACTCGCTGAAGCTCCTGGCAGCCCACTGC  
TTCATCCAGCACCAGTACCTCATGCCTGAGAATGTGGTGGAGGAGAAGACCAAGGCCATG  
GACCTGCACGCGGTCTTGGCGGAGCTTCCCCGGCCCCGCAGGCCCCCGCTGCAGTGCGG  
TACTCGGAAGTCTCCTTCATGGAGCTGGACAAATTCCTGGAGGATGTCAGGAATGGAATC  
TACCCACTGATGAACTTTGCAGCCACTCGACCCCTGGGGCTGCCCCGTGTGCTGGCCCCA  
CCCCCGGAGGAGGTCCAAAAGGCCAAGACCCCGACGCCAGAGCCCTTTGACTCTGAGACC  
AGAAAGGTTCATCCAGATGCAGTGCAACCTGGAGAGAAGCGAGGACAAGGCGCGCTGGCAT  
CTCACTCTGCTTCTGGTGCTGGAAGACCGGCTGCACCGGCAGCTGACCTACGACCTGCTC  
CCAACGGACAGCGCCCAGGACCTCGCCTCGGAGCTCGTGCACTATGGCTTCCTCCACGAG  
GACGACCGGATGAAGCTGGCCGCCTTCCTGGAGAGCACCTTCCTCAAGTACCGTGGGACC  
CAGGCCTGACCCGGAGCCCCAGCCCCAGGGGACCATGCCGGGGTGCTGCCCGGGCAGGCC  
ATGTTGGGGAGACTCCAGCACCGTGGGGCTGCCCTCCTCCATGCGCCTGGGAGCACAAAG  
GCCCCGGTAGTGAAGGAACCCCCCGTCTCCTGAGAGTGGGGCTGACCTGCCTTGGGCGC  
CGAGGGGTGGGGGGTGGGTGTGGGGGAGCCGTTAGGCCTCCAGGTCTTAGGATCAGG  
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GCCTGGCTGGGGCCACTGCCTCCTCAGCATGCAGGAGGCTGCCCTGTAGGGAACCCACAGC  
TCTGGGGCTTGGGGGTGAGGGTCAGCCCTGGACAGACCTCTGCCCAGGGAACCTGCTCCAT  
GGGGTCTGGGAGAGCAGCCATCCCCTGCTGGCACCATAGACCCACACAAGGAGCCTGCAC  
AGCAAGCCAGCGGTGACACACCTGCAGGTGTCAGGCATGGCACTGGGCACAACAGGGACC  
TGGCAGGAGAAACAGACCACAGAGAGGTCTGGAGTTGAGGCTGTTGTGAGCAAAGCCCCCT  
GGTCCCACACAGCTCTGCCCTAGAGCCACCTCTTTGACCCTTTACCCACCCTGAGACCAG  
AACTTGCAGCCCCCTCTGCAGATCTCCTCTGGCCACTGCAGCCCCCTCCAATGGGCTTTTTTC  
TCTCATGCATTCCCTGGCCTGGAGGCGTCAGGGACCCACATCCTCCCTGCTCCTCAGAC  
TCACAGCCCCCTCCATGTTACCTCCCGCACCTCCTCCCTGGGGCAGCTGCTCCCTGGGCCT  
CTGAGGATGTCAGCTCCTGGCTCCCTGCCTCTCTCCCACTCCACTCCTGGCTCAGTCTTA  
GAGATTTCTATGCCCTCATGGATTCTACCCCTGCCTTCCTGGCCTCTTGATTCTTGGCTT  
GCCTCTCCTCCAATTCCAAACTTAGTGAAATGGCCTTAAGCATTTTAAACTGTATGTATA  
CATTAGCGCATTTCATGCCTTTCTAAACGCATTTCAAATGTCAACCAGGAAGGCACACCAC

## FIGURE 2WW

TGTATTAGTTTTATACTGCCGCTGTAAATTTACCACAACTTAGTGACTTAACACAAAT  
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TGGCAGGCTGCCTTCCTTCCTGGAGGTTCTAGGGGAGACTCTGTCTCCTGCTCCTTCAGG  
CTGCTGGCAGAATCCACATCCTTTTCGGTGGCAGGGCCAAGGTCCCCACTTTCTTGCTGAC  
TGTAACCTAAGGCCACTTCCAGCTTGTAGAGGCTGCCTACATTCCTTGGCTCTTGGCCCC  
CTCCTCCATCTTCAGAGCTAGCAGGTTCACTGTGTGTACGAACCATTTCTCTGGTTCCT  
TGCAGACAGGAAAGGTTGTCCCTAAGGACTCATGAGATTAGGTTGGGCCCAGCCAGATAA  
TACATGATAATCTCCCTCCTCAAGGTTTTTAATATTAACACATCTGCAGGACACATTTT  
GCCATGTAACTAACATTCCTGCTTCCAGGGATTAAGGAATGAACCTCTTTTGTGGGG  
AAGGTGGCATTCTGTGACCACAGCACTCCAACCAAAGGCCAAAACCAAAGCAAGACT  
TACTAACGCATATCAAATAAATTAAAGGTACAAAATCGTGAATCTCAGTTATCTTAAATA  
TTCCAATACTATTTACAAAATTATTCAAATTCTCACGCCTTCCAACCTCAAATTAGCAAT  
CTAAAGTAATTTCCATATCCTAGATGGAAACCTCATGCTAAACTGTCTGATTATGCATG  
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AAGC

SEQ ID NO: 62\_AA103218\_M SGK034\_M

CCACGCGTCCGCACCAGAGTATGGCGAAGTCAATGATGGGACTGGCTTTGTGGACATCTT  
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CAGAGTCACAGAAGAGGCCATCGCTCGAGCCAGGCACTCACTGAGTGACCCCAACATGCG  
GGAATTCATCCTCTCCTGCCTGGCCCGGGACCTGCCCGCCGACCTCAGCCCACAACCT  
CCTCTTCCACCGAGTGCTCTTTGAGGTGCACTCGCTGAAGCTGCTGGCAGCTCACTGCTT  
CATCCAGCACCAGTACCTCATGCCTGAGAATGTGGTAGAGGAAAAGACCAAGGCCATGGA  
CCTCCATGCAGTTTTTGGCTGAGATGCCCGAGCCCCATGGACCCCCAATGCAGTGGCGGTA  
CTCAGAGGTCTCCTTCTTGGAGCTGGACAAATTCCTAGAGGATGTCAGGAACGGGATCTA  
TCCACTGATGAACTTTGCGGCTGCTCGGCCCTTGGGGCTTCCCCGTGTGTTGGCCCCACC  
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AACGGACAGTGCCCAGGACCTCGCTGCTGAACTAGTGCAATTATGGCTTCCTGCACGAGGA  
TGACAGGACAAAGCTAGCAGCCTTTCTGGAGACCACTTTTCTCAAGTACCGAGGGACGCA  
AGCGTGACCTTCCCAGTCCTGACGGCCCAGCAGAGATACAGGGGCTCAGGGTTGTCCACT  
TGGCAAAGAGCCCCACACTGCTCAAAGCTGCCTTCTGCCTGTGTTCCCTGGAACCTGAAC  
ACAGGCCCTGCTAGTGAAGACACCCCCACCCCCAGCTTTCTGCAGCAGTGTTGGGACCT  
GGGGTGGTGATGGAGCCCTGAGCCTGGACGAGAGTGGATACAGGTCAGTTAGGGGAACCG  
CTCCATCTGGTACTAGACAACAGCCATGCCTTCAGGTGGCATAGAAACCTAGGGAAGGAG  
CCTGAACTCAGGTGTACAGTGCTGGGCATCAGGCAGACCAGACCTGACCTGATTGGAGA  
ACTGTAGACTAGATAGCTTGGAGTTGAACCATGGCCAGGGAATTCCTTGGTCCTGCTCA  
GACCAGTCTGATCCCTTGACAGCCTGCCTTGAGCCCTCTTCTGATCTTCCACACTCTT  
GAGACCAGGACCTGTGTCCTCCCCAAAGCCCTTGGGAAGGATCTTCTATTATCATCCC  
TCTGGCCTAGGGGCTCAGGGGTCAGGCATCCTCCACATTCCTCCCTGGGGAAAGTTGTGT  
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TTCTTGAACCTGCCTCTCTCCCAACTTCAAACCAGGTCTTAAACGTTTTTTAAATGCATAT  
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TTTGAGACGACACACACACACACACACACACACACAGAGAGAGAGAGAGATTCTGTA  
CATCAAGTGTGATCCAGGCTCTCACTAGATTAATACCCAGGCTAAGTTCCCTTCTGGAAG  
CTGGGACTTACCTCCTGCTCCTTCAAGCTATTGGCAGAACTCACTTCCCTGCAATGGTAA  
GGCAGAAATCCCTATTTTCTCAACAGCTGCCAACTAAGAACCCCTCTCAGCTTCTAGAGG

## FIGURE 2XX

CCACCAACTTTTCTTAGTTCTTCTTTCTCCCCCTCAAGACCAGCAGCGTCAAGTTGAAT  
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GTAGGTTGGACCCACCAGGATAACCGAGGATGATCCCCTTCTCAGGGTCTATAGATGAAC  
CACACCTGCGCAGTTCCTTCTGCTGTCATCCTGGGCTTTGGTGCTTGGAGAACAGCCGTG  
GGCGGTGGGTGTTGTTACTGTGGTACCTACCATGCCATCTTAACCGAAACCAAGACCTAA  
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SEQ ID NO: 63\_NEK7\_H, N34132\_H

CACGAATCCGAGCCCGCTCGCCTCTCTCCAGCGAACCGACCATGTCTGGCGGCGCCGCAG  
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GGGCGGCCGCGACCACTACCACCACTGAGCACCCTTCTTCCGCGGAGCGTCATCTGCG  
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TCCCCGCGGCTGTCCCGCAGAGTGCTCCACCGGAGCCCCACCGGGAAGAGACCGTGACCG  
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GCGGCAGCGCCAAGGAGCCACAGGAGGAACGAGCCAGCAGCAGGATGATATCGAAGAGC  
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TCGCTTGGTGTGAACTGCAGGATCGAAAATTAACAAAGTCTGAGAGGCAGAGATTTAAAG  
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GAACACTTAAAACGTATCTGAAAAGGTTTAAAGTGATGAAGATCAAAGTTCTAAGAAGCT  
GGTGCCGTCAGATCCTTAAAGGTCTTCAGTTTCTTCATACTCGAACTCCACTTATCATTC  
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GAGACCTCGGTCTGGCAACCCTGAAGCGGGCTTCTTTTGCCAAGAGTGTGATAGGTACCC  
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GATATTCATCAAAGACCTTTTGAACCATGCCTTCTTCCAAGAGGAAACAGGAGTACGGG  
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AAGATATTAAGAAATTAAAGGGAAAATACAAAGATAATGAAGCTATTGAGTTTGTGTTTG  
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GTGAAGGTGATCACAAGACCATGGCTAAAGCTATCAAAGACAGAGTATCATTAAATTAAGA  
GGAAACGAGAGCAGCGGCAGTTGGTACGGGAGGAGCAAGAAAAACAAAAGCAGGAAGAGA  
GCAGTCTCAAACAGCAGGTAGAACAATCCAGTGCTTCCAGACAGGAATCAAGCAGCTCC  
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GGGTATATCCACCCTCAAGTGTGCAGCAGGGAATACAGCAGACAGCCCCCTCCTCAACAGA  
CAGTGCAGTATTCACTTTCACAGACATCAACCTCCAGTGAGGCCACTACTGCACAGCCAG  
TGAGTCAGCCTCAAGCTCCACAAGTCTTGCCCTCAAGTATCAGCTGGAAAACAGAGTACTC  
AGGGAGTCTCTCAGGTTGCTCCTGCAGAGCCAGTTGCAGTAGCACAGCCCCAAGCTACCC  
AGCCGACCACTTTGGCTTCTCTGTAGACAGTGCACATTCAAGTGTGCTTCAGGTATGA  
GTGATGGCAATGAGAACGTCCCATCTTCCAGTGGAAGGCATGAAGGAAGAACTACAAAAC

## FIGURE 2YY

GGCATTACCGAAAATCTGTAAGGAGTCGCTCTCGACATGAAAAAACTTCACGCCCAAAAT  
TAAGAATTTTGAATGTTTCAAATAAAGGAGACCGAGTAGTAGAATGTCAATTAGAGACTC  
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CAACAATTATGGTGAACAATGACTTTATTCTAGCAATAGAGAGAGAGTCTGTTTGTGGATC  
AAGTGCAGAGAAATTATTGAAAAAGCTGATGAAATGCTCAGTGAGGATGTCAGTGTGGAAC  
CAGAGGGTGATCAGGGATTGGAGAGTCTACAAGGAAAGGATGACTATGGCTTTTCAGGTT  
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TAGGCATTCTTACCAGTTCTTTAACTCAAGTTGTTTCTGCGGGAAGGCGGTTTATAG  
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CCCTTAGTCTACAACAGGCCTTTTCTGAACTTAGACGTGCCCAAATGACAGAAGGACCCA  
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TAAGTAGCATTGCTGGAGTCCAACCACAGCAGCAGCCACAGCACCAGTCCCTGCAACAA  
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CAGGCAGCACTACTGTGGGAGCCACATTAACATCAGTTTCTACCACCACTTCATTCCCAA  
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GAGATAAACATCTCAAAGAGATTCAAGGACCTGCAGAGTCGCCAGAAGCATGAAATTGAAT

## FIGURE 2ZZ

CTTTGTATACCAAACCTGGGCAAGGTGCCCCCTGCTGTTATTATTCCCCCAGCTGCTCCCC  
TTTCAGGGAGAAGACGACGACCCACTAAAAGCAAAGGCAGCAAATCTAGTCGAAGCAGTT  
CCTTGGGGAATAAAAGCCCCCAGCTTTCAGGTAACCTGTCTGGTCAGAGTGCAGCTTCAG  
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GTGAAAAGGGAAGTGGAGTGATAATGAGAATCGGTGGGCTCACTGCTCCCATTAGGTGAA  
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TCAAATAACAAGTTATCTACAAATTTCAATGTAACTTTCTGGTAGAAGTGCTTCTTCAT  
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GAGAGAAATCAGCCAGACACGGTGGCGTACACCTGTAATCCCAGCACTTGGGAGGCCGA  
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SEQ ID NO: 64\_BCON3\_H

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GGGGGAGTCCCAGACAGTACTTAGCAGTGGCTCAGACCCAAAGGTAGAATCCTCATCTTC  
AGCTCCTGGCCTGACATCAGTGTCACCTCCTGTGACCTCCACAACCTCAGCTGCTTCCCC  
AGAGGAAGAAGAAGAAAGTGAAGATGAGTCTGAGATTTTGGAAGAGTCGCCCTGTGGGCG  
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CCTGGCCATGGATACAGAGGAAGGTGTAGAGGTGTGTGGAATGAGGTACAGTTCTCTGA  
ACGCAAGAACTACAAGCTGCAGGAGGAAAAGGTTCTGTCTGTGTTTGATAATCTGATTCA  
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GACCTGTGACACCATCTTCATCCAGCACAAACGGACTCATCAAGATTGGCTCTGTGGCTCC  
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TGCACCAGAGTATGGAGAAGTCACTAATGTGACAACAGCAGTGGACATCTACTCCTTTGG  
CATGTGTGCACTGGAGATGGCAGTGCTGGAGATTACAGGGCAATGGAGAGTCTCATATGT  
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## FIGURE 2AAA

CATTCAAAAGTGCCTGCAGTCTGAGCCTGCTCGCAGACCAACAGCCAGAGAACTTCTGT  
CCACCCAGCATTGTTTGAAGTGCCCTCGCTCAAACCTCCTTGCGGCCCCACTGCATTGTGGG  
ACACCAACACATGATCCCAGAGAACGCTCTAGAGGAGATCACCAAAAACATGGATACTAG  
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TGTCGTGCCCCCTCTGTCAAGACTCCGACACCTGAACCAGCTGAGGTGGAGACTCGCAA  
GGTGGTGCTGATGCAGTGCAACATTGAGTCGGTGGAGGAGGGAGTCAAACACCACCTGAC  
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AGTATTACCCTGTGAAGCCCCCTCCCTCCTTTATTATTAGGAGGGCTGGGGGGGCTCCC  
TGGTTCTGAGCATCATCCTTTCCCCTCCCCTCTCTCCTCCCCTCTGCACTTTGTTTACT  
TGTTTTGCACAGACGTGGGCCTGGGCCTTCTCAGCAGCCGCTTCTAGTTGGGGGCTAGT  
CGCTGATCTGCCGGCTCCCGCCAGCCTGTGTGGAAAGGAGGCCACGGGCACTAGGGGA  
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GCT

SEQ ID NO: 65\_AA711829\_M

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TACTTGTTTTGCACAGACGTGGGCCTGGGCCTTCTCAGCAGCCACCTTCTAGCTGGGGGC  
TAGTAGCTGACCTGCTGCCTCCTGCCCTACTTGTGTGGACAGGAGGCCACGGGCACTGG  
GGAAGCTGAGTTCTACAATCCCGCTGGGGCGCATGGGCAGGAGAGAAAGGTGGTGTGCA  
GGGGTGGCCCCCGGGGGGGGCATTGCAATCACCTCAGTTGCTGTGTAATAAAGTCTAC  
TTTTTGCT



## FIGURE 2BBB

SEQ ID NO: 66\_AA099102\_H

ATGTCATCATGTGTCTCTAGCCAGCCCAGCAGCAACCGGGCCGCCCCCAGGATGAGCTG  
GGGGGCAGGGGCAGCAGCAGCAGCGAAAGCCAGAAGCCCTGTGAGGCCCTGCGGGGCCTC  
TCATCCTTGAGCATCCACCTGGGCATGGAGTCCTTCATTGTGGTCACCGAGTGTGAGCCG  
GGCTGTGCTGTGGACCTCGGCTTGGCGCGGGACCGGCCCTGGAGGCCGATGGCCAAGAG  
GTCCCCCTTGACACCTCCGGGTCCCAGGCCCGGCCACCTCTCCGGTCGCAAGCTGTCT  
CTGCAAGAGCGGTCCCAGGGTGGGCTGGCAGCCGGTGGCAGCCTGGACATGAACGGACGC  
TGCATCTGCCCCTCCCTGCCCTACTCACCCGTGAGCTCCCCGAGTCCTCGCCTCGGCTG  
CCCCGGCGGGCCGACAGTGGAGTCTCACCACGTCTCCATCACGGGTATGCAGGACTGTGTG  
CAGCTGAATCAGTATACCCTGAAGGATGAAATTGGAAAGGGCTCCTATGGTGTCTGCAAG  
TTGGCCTACAATGAAAATGACAATACCTACTATGCAATGAAGGTGCTGTCCAAAAGAAG  
CTGATCCGGCAGGCCGCTTTTCCACGTGCGCCTCCACCCCGAGGCACCCGGCCAGCTCCT  
GGAGGCTGCATCCAGCCCAGGGGCCCATTTAGCAGGTGTACCAGGAAATTGCCATCCTC  
AAGAAGCTGGACCACCCCAATGTGGTGAAGCTGGTGGAGGTCTGGATGACCCCAATGAG  
GACCATCTGTACATGGTGTTCGAAGTGGTCAACCAAGGGCCCGTGATGGAAGTGCCACC  
CTCAAACTCTCTGAAGACCAGGCCGTTTCTACTTCCAGGATCTGATCAAAGGCATC  
GAGTACTTACACTACCAGAAGATCATCCACCGTGACATCAAACCTTCCAACCTCCTGGTC  
GGAGAAGATGGGCACATCAAGATCGCTGACTTTGGTGTGAGCAATGAATTCAAGGGCAGT  
GACGCGCTCCTCTCCAACCTACGTGGGCACGCCCGCTTCATGGCTCCCGAGTCGCTCTCT  
GAGACCCGCAAGATCTTCTCTGGGAAGGCCAAGGATGTTTGGGCCATGGGTGTGACACTA  
TACTGCTTTGTCTTTGGCCAGTGCCCATTCATGGACGAGCGGATCATGTGTTTACACAGT  
AAGATCAAGAGTCAGGCCCTGGAATTTCCAGACCAGCCCGACATAGCTGAGGACTTGAAG  
GACCTGATCACCCGTATGCTGGACAAGAACCCCGAGTCGAGGATCGTGGTGGCCGAAATC  
AAGCTGCACCCCTGGGTACGAGGCATGGGGCGGAGCCGTTGCCGTCCGAGGATGAGAAC  
TGCACGCTGGTCAAGTGACTGAAGAGGAGGTGAGAACTCAGTCAAACACATTCCCAGC  
TTGGCAACCGTGATCCTGGTGAAGACCATGATACGTAAACGCTCCTTTGGGAACCCATTC  
GAGGGCAGCCGGCGGGAGGAACGCTCACTGTGAGCGCCTGGAAACTTGCTCACCAAAAA  
CCAACCAGGGAATGTGAGTCCCTGTCTGAGCTCAAGGAAGCAAGGCAGCGAAGACAACCT  
CCAGGGCACCAGCCCGCCCCCGTGGGGGAGGAGGAAGTGCTCTTGTGAGAGGCAGTCCC  
TGCGTGGAAAGTTGCTGGGCCCCCGCCCCGGCTCCCCCGCACGCATGCATCCACTGCGG  
CCGGAGGAGCCATGGAGCCCGAGTAG

SEQ ID NO: 67\_5R69\_17\_2\_H

CCGGGATGTGAGCCTGGTGGTTGGCAGCTGGAGCCACGTCCGAGGGGGAAGTGTGCGAGC  
ATTCTCTGCAGGCATCACAGACCTGAGGCAGTGGCCTCCGGAGGGCACTGGACAGAAACA  
GCCATCCAAGTGGCTGAGTGGAGGGACCTGCTCAAGTGCAGCTGCAGTGGCCGGGGTTT  
CCCTCAGGTAGGGATCGGGGCGCCTTGTGCGCCGACCCACGTGTGGCGTCCGGTACAGT  
CAGCAGAGTGCAGGGTGCGGGCACCAGGAAAGGGGGCGCAGGGGAACCTCCCGCGGGCCTC  
GCGTTTGCAAACCTTCTCGCCTGGGCAGGAGGCGGTGCTGGGAAAGAAGGTGGAAGAGCGA  
GCTTTTTTGAACTGTGCACGGGACAGATTGGACGCACACCCCTCGGGAGGCGCGAAGGCA  
TGGAATAATTTGAAGCATATTATCACCCCTTGGCCAGGTATCCACAAACGGTGTGAAGAGA  
TGAAATACTGCAAGAAACAGTGCCGGCGCCTGGGCCACCGCGTCTCGGCCTGATCAAGC  
CTCTGGAGATGCTCCAGGACCAAGGAAAGAGGAGCGTGCCCTCTGAGAAGTTAACCACAG  
CCATGAACCGCTTCAAGGCTGCCCTGGAGGAGGCTAATGGGGAGATAGAAAAGTTTCAAGC  
ATAGATCCAATATCTGCAGGTTTCTAACAGCAAGCCAGGACAAAATACTCTTCAAGGACG  
TGAACAGGAAGCTGAGTGTCTGGAAGGAGCTCTCGCTGTTACTTTCAGGTTGAGCAAC  
GCATGCCTGTTTACCCATAAGCCAAGGAGCGTCTGGGCACAGGAAGATCAGCAGGATG  
CAGACGAAGACAGGCGAGCTTTCCAGATGCTAAGAAGAGATAATGAAAAAATAGAAGCTT  
CACTGAGACGATTAGAAATCAACATGAAAGAAATCAAGGAACTTTGAGGCAGTGTAAAGT  
TATCATGTGCCCTGCTGTTTCTGATGGCCCCCAACTAGAAGTCATCAGTTTACTGGGAC



## FIGURE 2CCC

CCCAGCCTCCCGCTACCCCTGCATTTGTCCATTTTCTGTGCTGGATGGCTGGAAGCAGCC  
CACAGGTTTGGGGATCCATTCATGGCTAGCCCAGGCTTCTGTCCATGGAATAACATGTGG  
AGAGAGCTTCTTGACCAGTAAGATACCTTCTAGCAGCTGTCAAAGTACTTAAAAACCTCT  
ATGAATAGAATCAAAGCTTCAGTTCAGTTGCTGAATTTCCAAGAAGAAATTCAAATCAA  
TTTAAATGCCCACTCATTTCATTTCATCAACAAAACCTGTGAGTATCTGGTTTATGCCAGA  
GGCCATGCAAAGAGGTAACATAAGATGCAGAGAAGGACACTGCCTTCCAGGAGCTCACGGG  
GTGGAGGAGGAAAGAGGAAAGACAGACAGTGAACACACAACAGCAAGGTTACTGAGCTTG  
AACTATGTCCCTAACTACTAGATCTGAAATGACTACGCCAGATGCCAGATGCTCAAGTGC  
CAAGCTCTGGGTAACAGGAATAGACATCCTTCCAGGATGAGAGAGATGAGTCTGGATGAG  
GGTTAAGGCTGGAGGGACAGGCGGGATTTGAAGAGGAGGGAAAGGAAGTGGATGACACAT  
TCTGTTAACTGTCCAGCTGTGTCTCTACTGGTCACTCAGAGGCACGGGAGCCGCTCCCTT  
GGGCTGAGTCCATCAGAAGCCCCAGCCACCACCAGCTCTGGTTCATGTAGTAGAGCTTCC  
CACTCACACATCACAAATATGCCACCTCCCTTAGGACCCCTTCTCTGCTCATTGACTCT  
TTTGTCTTCTTCTCTCGGGGTGAGGTGAGATTTACCACCAAATGCATGCAGGAGAT  
CCCCAAGAGCAAATCAAGGAGATCAAGAAGGAGCAGCTTTCAGGATCCCCGTGGATTCT  
GCTAAGGGAAAATGAAGTCAGCACACTTTATAAAGGAGAATACCACAGAGCTCCAGTGGC  
CATAAAAGTATTCAAAAACTCCAGGCTGGCAGCATTGCAATAGTGAGGCAGACTTTCAA  
TAAGGAGATCAAAACCATGAAGAAATTGCAATCTCCCAACATCCTGCGTATATTTGGGAT  
TTGCATTGATGAAACAGTGAATCCGCTCAATTCTCCATTGTCATGGAGTACTGTGAACT  
CGGGACCCTGAGGGAGCTGTTGGATAGGGAAAAAGACCTCACACTTGGCAAGCGCATGGT  
CCTAGTCTTGGGGGAGCCCGAGGCTATACCGGCTACACCATTGAGAAGCACCTGAACT  
CCACGGAAAAATCAGAAGCTCAAACCTTCTGGTAACTCAAGGCTACCAAGTGAAGCTTGC  
AGGATTTGAGTTGAGGAAAACACAGACTTCCATGAGTTTGGGAACTACGAGAGAAAAGAC  
AGACAGAGTCAAATCTACAGCATATCTCTCACCTCAGGAACTGGAAGATGTATTTTATCA  
ATATGATGTAAAGTCTGAAATATACAGCTTTGGAATCGTCCTCTGGGAAATCGCCACTGG  
AGATATCCCGTTTCAAGGTGAAGAATGTGAAGACTGGCTCAGCCAGTGGCTGTAATTTCTG  
AGAAGATCCGCAAGCTGGTGGCTGTGAAGCGGCAGCAGGAGCCACTGGGTGAAGACTGCC  
CTTCAGAGCTGCGGGAGATCATTGATGAGTGCCGGGCCCATGATCCCTCTGTGCGGCCCT  
CTGTGGATGAAATCTTAAAGAACTCTCCACCTTTTCTAAGTAGTGTATCAAATCTAAA  
CCAAGGAGTCTCTGGACAAGAAGCTGGGAGAGGCACGAACTGGACATCTCTCTCTCAT  
ATCCTTCGGCATTGGGTTATCTATGGGTGCAAGGAGTGGGCACGCTTCTCTGTTACAAAT  
AGAAAACGATTCCAGTCATACAGGACACATCCCACTCCAAATGATATTTCCAAAAACATA  
CCTCTGACAGTAACTTTGATAGATGGTTTGTCAAATGTATCTTTCTGGGTATCCACACCT  
CTTGGCAATGAAATTTGCAGCTCCTCCCTTCCATAAATGAAGTCTCTTTCCCCACCATT  
GAATCTGGGCTGGCACTGTGACTTGATTTGATCAATAGAATGTGGAAGAAGTGAATGTAT  
GCCAGTTCCAAGCCTAGGTTTCAAGAGGCCTTATAAATGTCTGTTGGAACCTTACCCAGC  
CATGGACATGTTGAGTGAGCATGCTGGAGAATGAGAGACCACATGAAGCAGAAACATGCT  
TTCCTAGCTGAAGTCATACTAGCCCAACCAACATGGCAGCTAACACATGAATGAGGCCAA  
TCAAGACCAGAAGAACCACTCAAGCAGATCCCAGCCCAAATTGCCCATTCACACAATCAG  
GAGCTAAATAAATTACTGTTGTCTTTT

SEQ ID NO: 68\_H85811\_H

CGCCCGGCCCCCTCCCCGGCGCCGGCCACGGGAGGCGGTGATGCGGGCGCGGGCGGCCT  
CGGCTGCGCCGAGAGCGGAGACACAGGCTCAAGATGGCAGATTCGACTGAGGCTGGGGG  
GGCCGAGCTCGCGCGCCGCTTTCCCGTCCCGTTGCCATGAACCGCGGACACCCCGGCCC  
CGATGGCCCCCGTGTACGAAGGTATGGCCTCACATGTGCAAGTTTTCTCCCTCACACCC  
TTCAATCAAGTGCCTTCTGTAGTGTGAAGAACTGAAAATAGAGCCGAGTTCCAAGTGGG  
ACATGACTGGGTACGGCTCCACAGCAAAGTGTATAGCCAGAGCAAGAACATCCCCCTGT  
CGCAGCCAGCCACCACAACCGTCAGCACCTCCTTGCCGGTCCCAAACCCAAGCCTACCTT  
ACGAGCAGACCATCGTCTTCCCAGGAAGCACCGGGCACATCGTGGTCACCTCAGCAAGCA

## FIGURE 2DDD

GCACTTCTGTCACCGGGCAAGTCCTCGGCGGACCACACAACCTAATGCGTCGAAGCACTG  
TGAGCCTCCTTGATACCTACCAAAAATGTGGACTCAAGCGTAAGAGCGAGGAGATCGAGA  
ACACAAGCAGCGTGAGATCATCGAGGAGCATCCACCCATGATTCAGAATAATGCAAGCG  
GGGCCACTGTGCGCCACTGCCACCACGTCTACTGCCACCTCCAAAAACAGCGGCTCCAACA  
GCGAGGGCGACTATCAGCTGGTGCAGCATGAGGTACTGTGCTCCATGACCAACACCTACG  
AGGTCTTAGAGTTCTTGCGCCGAGGGACGTTTGGGCAAGTGGTCAAGTGCTGGAAACGGG  
GCACCAATGAGATCGTAGCCATCAAGATCCTGAAGAACCACCCATCCTATGCCCCGACAAG  
GTCAGATTGAAGTGAGCATCCTGGCCCGGTTGAGCACGGAGAGTGCCGATGACTATAACT  
TCGTCCGGGCTACGAATGCTTCCAGCACAAGAACCACACGTGCTTGGTCTTCGAGATGT  
TGGAGCAGAACCTCTATGACTTTCTGAAGCAAAAACAGTTTAGCCCCCTTGCCCCCTCAAAT  
ACATTCGCCCAGTTCTCCAGCAGGTAGCCACAGCCCTGATGAAACTCAAAGCCTTAGGTC  
TTATCCACGCTGACCTCAAACCAGAGAACATCATGCTGGTGGATCCATCTAGACAACCAT  
ACAGAGTCAAGGTCATCGACTTTGGTTCAGCCAGCCACGTCTCCAAGGCTGTGTGCTCCA  
CCTACTTGACGTCCAGATATTACAGGGCCCCCTGAGATCATCCTTGGTTTACCATTTTGTG  
AGGCAATTGACATGTGGTCCCTGGGCTGTGTTATTGCAGAATTGTTCCCTGGGTGGCCGT  
TATATCCAGGAGATTCCGAGTATGATCAGATTCGGTATATTTTCAAAACACAGGGTTTGC  
CTGCTGAATATTTATTAAGCGCCGGGACAAAGACAACCTAGGTTTTTCAACCGTGACACGG  
ACTCACCATATCCTTTGTGGAGACTGAAGACACCAGATGACCATGAAGCAGAGACAGGGA  
TTAAGTCAAAGAAGCAAGAAAGTACATTTTCAACTGTTTAGATGATATGGCCCAGGTGA  
ACATGACGACAGATTTGGAAGGGAGCGACATGTTGGTAGAAAAGGCTGACCGCGGGAGT  
TCATTGACCTGTTGAAGAAGATGCTGACCATTGATGCTGACAAGAGAATCACTCCAATCG  
AAACCCTGAACCATCCCTTTGTCACCATGACACACTTACTCGATTTTCCCCACAGCACAC  
ACGTCAAATCATGTTTCCAGAACATGGAGATCTGCAAGCGTCGGGTGAATATGTATGACA  
CGGTGAACCAGAGCAAAACCCCTTTCATCACGCACGTGGCCCCCAGCACGTCCACCAACC  
TGACCATGACCTTTAACAACCAGCTGACCACTGTCCACAACCAGCCCTCAGCGGCATCCA  
TGGCTGCAGTGGCCCAGCGGAGCATGCCCTGCAGACAGGAACAGCCCAGATTTGTGCCC  
GGCCTGACCCGTTCCAGCAAGCTCTCATCGTGTGTCCCCCGGCTTCCAAGGCTTGCAGG  
CCTCTCCCTCTAAGCACGCTGGCTACTCGGTGCGAATGGAAAATGCAGTTCCTATCGTCA  
CTCAAGCCCCAGGAGCTCAGCCTCTTCAGATCCAACCAGGTCTGCTTGCCCAGCAGGCTT  
GGCCAAGTGGGACCCAGCAGATCCTGCTTCCCCAGCATGGCAGCAACTGACTGGAGTGG  
CCACCCACACCTCAGTGCAGCATGCCACCGTGATTCCCGAGACCATGGCAGGCACCCAGC  
AGCTGGCGGACTGGAGAAATACGCATGCTCACGGAAGCCATTATAATCCCATCATGCAGC  
AGCCTGCACTATTGACCGGTCATGTGACCTTCCAGCAGCACAGCCCTTAAATGTGGGTG  
TGGCCCACGTGATGCGGCAGCAGCCAACCAGCACCTCCTCCCGGAAGAGTAAGCAGC  
ACCAGTCATCTGTGAGAAATGTCTCCACCTGTGAGGTGTCTCCTCTCAGGCCATCAGCT  
CCCCACAGCGATCCAAGCGTGTCAAGGAGAACACACCTCCCCGCTGTGCCATGGTGCACA  
GTAGCCCGGCTGCAGCACCTCGGTACCTGTGGGTGGGGCGACGTGGCCTCCAGCACCA  
CCCGGGAACGGCAGCGGCAGACAATTGTCAATCCCCGACACTCCCAGCCCCACGGTCAGCG  
TCATCACCATCAGCAGTGACACGGACGAGGAGGAGGAACAGAAACACGCCCCACCAGCA  
CTGTCTCCAAGCAAAGAAAAACGTCAATCAGCTGTGTACAGTCCACGACTCCCCCTACT  
CCGACTCCTCCAGCAACACCAGCCCCCTACTCCGTGCAGCAGCGTGCTGGGCACAACAATG  
CCAATGCCTTTGACACCAAGGGGAGCCTGGAGAATCACTGCACGGGGAACCCCCGAACCA  
TCATCGTGCCACCCCTGAAAACCCAGGCCAGCGAAGTATTGGTGGAGTGTGATAGCCTGG  
TGCCAGTCAACACCAGTCACCACTCGTCCTCCTACAAGTCCAAGTCTCCAGCAACGTGA  
CCTCCACCAGCGGTCACTCTTCAGGGAGCTCATCTGGAGCCATCACCTACCGGCAGCAGC  
GGCCGGGCCCCCACTTCCAGCAGCAGCAGCCACTCAATCTCAGCCAGGCTCAGCAGCACA  
TCACCACGGACCGCACTGGGAGCCACCGAAGGCAGCAGGCCTACATCACTCCACCATGG  
CCCAGGCTCCGTACTCCTTCCCGCACAAACAGCCCCAGCCACGGCACTGTGCACCCGCATC  
TGGCTGCAGCCGCTGCCGCTGCCACCTCCCCACCCAGCCCCACCTCTACACCTACACTG  
CGCCGGCGGCCCTGGGCTCCACCGGCACCGTGGCCACCTGGTGGCCTCGCAAGGCTCTG

## FIGURE 2EEE

CGCGCCACACCGTGCAGCACACTGCCTACCCAGCCAGCATCGTCCACCAGGTCCCCGTGA  
GCATGGGCCCCCGGGTCTGCCCTCGCCCACCATCCACCCGAGTCAGTATCCAGCCCAAT  
TTGCCCACCAGACCTACATCAGCGCCTCGCCAGCCTCCACCGTCTACACTGGATACCCAC  
TGAGCCCCGCCAAGGTCAACCAGTACCCTTACATATAAACACTGGAGGGGAGGGAGGGAG  
GGAGGGAGGGAGAGAATGGCCCCGAGGGAGGGAGGGAGAGAAGGAGGGAGGGCGTCTCTGGGA  
CCGTGGGCGCTGGCCTTTTATACTGAAGATGCCGCACACAAACAATGCAAACGGGGCAGG  
GGCGGGGGGGGGGGGGCAGAGGGCAGGGGGACGGGTCTGGGACACCAGTGAAACTTGAACC  
GGGAAGTGGGAGGACGTAGAGCAGAGAAGAGAACATTTTTTAAAAGGAAGGGATTAAAGAG  
GGTGGGAATCTATGGTTTTTATTTTAAAAAAG

SEQ ID NO: 69\_DYRK3\_H

CGGGAGCGAAAGTGCCTGAGCTGCAGTGTCTGGTCGAGAGTACCCGTGGGAGCGTCGCG  
CCGCGGAGGCAGCCGTCCCGGCGTAGGTGGCGTGGCCGACCCGACCCCCAACTGGCGCCT  
CTCCCCGAGCGGGGTCCCGAGCTAGGAGATGGGAGGCACAGCTCGTGGGCCTGGGCGGAA  
GGATGCGGGGCCGCTGGGGCCGGGCTCCCGCCCCAGCAGCGGAGTTGGGGGATGGTGTG  
TATGACACCTTCATGATGATAGATGAAACCAAATGTCCCCCTGTTCAAATGTACTCTGC  
AATCCTTCTGAACCACCTCCACCCAGAAGACTAAATATGACCGCTGAGCAGTTTACAGGA  
GATCATACTCAGCACTTTTTGGATGGAGGTGAGATGAAGGTAGAACAGCTGTTTCAAGAA  
TTTGGCAACAGAAAATCCAATACTATTTCAGTCAGATGGCATCAGTGAATCTGAAAAATGC  
TCTCCTACTGTTTCTCAGGGTAAAAGTTTCAGATTGCTTGAATACAGTAAATCCAACAGT  
TCATCCAAGGCACCCAAAGTGGTGCCTCTGACTCCAGAACAGCCCTGAAGCAATATAAA  
CACCACCTCACTGCCTATGAGAACTGGAAATAATTAATTATCCAGAAATTTACTTTGTA  
GGTCCAAATGCCAAGAAAAGACATGGAGTTATTGGTGGTCCCAATAATGGAGGGTATGAT  
GATGCAGATGGGGCCTATATTTCATGTACCTCGAGACCATCTAGCTTATCGATATGAGGTG  
CTGAAAATTATTGGCAAGGGGAGTTTTGGGCAGGTGGCCAGGGTCTATGATCACAACTT  
CGACAGTACGTGGCCCTAAAAATGGTGCCTCAATGAGAAGCGCTTTCATCGTCAAGCAGCT  
GAGGAGATCCGGATTTTGGAGCATCTTAAGAAACAGGATAAACTGGTAGTATGAACGTT  
ATCCACATGCTGGAAAGTTTCACATTCCCGAACCATGTTTGCATGGCCTTTGAATTGCTG  
AGCATAGACCTTTATGAGCTGATTAAAAAAATAAGTTTCAGGGTTTTAGCGTCCAGTTG  
GTACGCAAGTTTGGCCAGTCCATCTTGCAATCTTTGGATGCCCTCCACAAAAATAAGATT  
ATTCAGTGCATCTGAAGCCAGAAAACATTCTCCTGAAACACCACGGGCGCAGTTCAACC  
AAGGTCATTGACTTTGGGTCCAGCTGTTTCGAGTACCAGAAGCTCTACACATATATCCAG  
TCTCGGTTCTACAGAGCTCCAGAAATCATCTTAGGAAGCCGCTACAGCACACCAATTGAC  
ATATGGAGTTTTTCGCTGCATCCTTGCAAGACTTTTAACAGGACAGCCTCTCTTCCCTGGA  
GAGGATGAAGGAGACCAGTTGGCCTGCATGATGGAGCTTCTAGGGATGCCACCACCAAAA  
CTTCTGGAGCAATCCAAACGTGCCAAGTACTTTATTAATTCCAAGGGCATAACCCGCTAC  
TGCTCTGTGACTACCCAGGCAGATGGGAGGGTTGTGCTTGTGGGGGGTCTGCTCACGTAGG  
GGTAAAAAGCGGGGTCCCCCAGGCAGCAAAGACTGGGGGACAGCACTGAAAGGGTGTGAT  
GACTACTTGTATTATAGAGTTCTTGAAAAGGTGTCTTCACTGGGACCCCTCTGCCCGCTTG  
ACCCAGCTCAAGCATTAAAGACACCCTTGGATTAGCAAGTCTGTCCCCAGACCTCTCACC  
ACCATAGACAAGGTGTGAGGGAAACGGGTAGTTAATCCTGCAAGTGCTTTCCAGGGATTG  
GGTTCTAAGCTGCCTCCAGTTGTTGGAATAGCCAATAAGCTTAAAGCTAACTTAATGTCA  
GAAACCAATGGTAGTATACCCCTATGCAGTGTATTGCCAAAAGTATTAGCTAGTGGACA  
GAGATATGCCCAGAGATGCATATGTGTATATTTTTATGATCTTACAAACCTGCAAAATGGA  
AAAAATGCAAGCCATTGGTGGATGTTTTTGTAGAGTAGACTTTTTTTAAACAAGACAA  
AACATTTTTATATGATTATAAAAGAATTCTTCAAGGGCTAATTACCTAACAGCTTGTAT  
TGCCCATCTGGAATATGCATTAAATGACTTTTTTATAGGTCA

## FIGURE 2FFF

SEQ ID NO: 70\_AA589241\_M DYRK3\_M

CCACGCGTCCGGAGTTGCTAGGAATGCCACCGCAGAACTTCTGGAGCAATCCAAGCGTG  
CCAAGTACTTTTATTAACCTCCAAAGGCTTGCCTCGATACTGCTCCGTATCTACCCAGACGG  
ACGGGAGGGTGGTGCTTCTCGGGGGTTCGCTCACGCAGGGGTAAAAAGCGAGGGCCCGCCAG  
GCAGCAAAGACTGGGCAACCGCACTGAAGGGCTGTGGTGACTACTTGTTCATAGAGTTTC  
TGAAACGATGCCTCCAGTGGGACCCCTCTGCCCCCTCACCCCGGCTCAAGCATTAAGAC  
ATCCTTGGATTAGCAAGTCTACACCCAAACCTCTCACCATGGACAAGGTGCCAGGGAAGC  
GGGTAGTTAACCTACAAATGCTTTCCAGGGACTGGGTTCGAAGCTGCCTCCAGTCGTTG  
GGATAGCCAGTAAGCTTAAAGCTAACCTAATGTCCGAAACCAGTGGTAGTATACCTCTGT  
GCAGTGTATTGCCAAAGCTGATTAGCTAGTGACCCTCAGAGACTGATACATATCATAT  
GTATTTTAAATTACCTTGCAAACATGCAAATGGAAAACGGAATAATTGAAGCCCATTAC  
TGATGGATATGTTTTGTAGACTTTTTTTTAAACAAGGCAGAACATTTTATATGACTAT  
AAAAGAACGCTTCAAGGGCTAATGTCAAACCAGCTTGTATTGGCCATCTGGAGTATACAT  
TAAATGACTTTTTTCATAGGTC

SEQ ID NO: 71\_5R72\_16\_2\_H

GTCGAGGCGCAGCGCTGCCATGGCTGGGGGCCGTGGGGCCCCGGGCGCGGCCGGGACGA  
GCCTCCGGAGAGCTACCCGCAACGACAGGACCACGAGCTACAGGCCCTGGAGGCCATCTA  
CGGCGCGGACTTCCAAGACCTGCGGCCGGACGCTTGCAGGACCGGTCAAAGAGCCCCCTGA  
AATCAATTTAGTTTTGTACCCTCAAGGCCTAACTGGTGAAGAAGTATATGTAAAAGTGGA  
TTTGAGGGTTAAATGCCACCTACCTATCCAGATGTAGTTCCTGAAATAGAGTTAAAAAA  
TGCCAAAGGTCTATCAAATGAAAGTGTCAATTTGTAAAATCTCGCCTAGAAGAACTGGC  
CAAGAAACACTGTGGGGAGGTGATGATCTTTGAACTGGCTTACCACGTGCAGTCATTTCT  
CAGCGAGCATAACAAGCCCCCTCCCAAGTCTTTTCATGAAGAAATGCTGGAAAGGCGGGC  
TCAGGAGGAGCAGCAGAGGCTGTTGGAGGCCAAGCGGAAAGAAGAGCAGGAGCAACGTGA  
AATCCTGCATGAGATTGAGAGAAGGAAAGAAGAGATAAAAAAGAGAAAAAAGGAAAGA  
AATGGCTAAGCAGGAACGTTTGGAAATTGCTAGTTTGTCAAACCAAGATCATACCTCTAA  
GAAGGACCCAGGAGGACACAGAACGGCTGCCATTCTACATGGAGGCTCTCCTGACTTTGT  
AGGAAATGGTAAACATCGGGCAAACCTCCTCAGGAAGGTCTAGGCGAGAACGTCAGTATTC  
TGTATGTAATAGTGAAGATTCTCCTGGCTCTTGTGAAATTCTGTATTTCAATATGGGGAG  
TCCTGATCAGCTCATGGTGCACAAAGGGAAATGTATTGGCAGTGATGAACAACTGGAAA  
ATTAGTCTACAATGCTTTGGAAACAGCCACTGGTGGCTTTGTCTTGTGTATGAGTGGGT  
CCTTCAGTGGCAGAAAAAATGGGTCCATTCCCTTACCAGTCAAGAAAAAGAGAAGATTGA  
TAAGTGCAAAAAGCAGATTCAAGGAACAGAAACAGAATTCAACTCACTGGTAAAAATTGAG  
CCAATCCAAATGTAGTACGCTACCTTGCAATGAATCTCAAAGAGCAAGACGACTCCATCGT  
GGTGGACATTTTGTAGTGGAGCACATTAGTGGGGTCTCTCTTGCTGCACACCTGAGCCACTC  
AGGCCCCATCCCTGTGCATCAGCTTCGCAGGTACACAGCTCAGCTCCTGTGAGGCCTTGA  
TTATCTGCACAGCAATTCTGTGGTGCATAAGGTCCTGAGTGCATCTAATGTCTTGGTGGGA  
TGCAGAAGGCACCGTCAAGATTACGGACTATAGCATTTCTAAGCGCCTCGCAGACATTTG  
CAAGGAGGATGTGTTTGAGCAAACCCGAGTTCGTTTTAGTGACAATGCTCTGCCTTATAA  
AACGGGGAAGAAAGGAGATGTTTGGCGTCTTGGCCTTCTGCTGCTGTCCCTCAGCCAAGG  
ACAGGAATGTGGAGAGTACCCTGTGACCATCCCTAGTGACTTACCAGCTGACTTTCAAGA  
TTTTCTAAAGAAATGTGTGTGCTTGGATGACAAGGAAAGATGGAGTCCCCAGCAGTTGTT  
GAAACACAGCTTTATAAATCCCCAGCCAAAAATGCCTCTAGTGGAACAAAGTCCTGAAGA  
TTCTGGAGGACAAGATTATGTTGAGACTGTTATTCCTAGCAACCGGCTACCCAGTGCTGC  
CTTCTTTAGTGAGACACAGAGACAGTTTTCCCGATACTTCATTGAGTTTGAAGAATTACA  
ACTTCTTGGTAAAGGAGCTTTTGGAGCTGTCATCAAGGTGCAGAACAAAGTTGGACGGCTG  
CTGCTACGCACTGAAGCGCATCCCCATCAACCCGGCCAGCCGGCAGTTCGCGAGGATCAA  
GGGCGAAGTGACACTGCTGTACGGCTGCACCATGAGAACATTGTGCGCTACTACAACGC  
CTGGATCGAGCGGCACGAGCGGCCGGCGGGACCGGGGACCGCCGCCCCCGGACTCCGGGCC

## FIGURE 2GGG

CCTGGCCAAGGATGACCGAGCTGCACGCGGGCAGCCGGCGAGCGACACAGACGGCCTGGA  
CAGCGTAGAGGCCGCGCGCCGCCACCCATCCTCAGCAGCTCGGTGGAGTGGAGCACTTC  
GGGCGAGCGCTCGGCCAGTGCCCGTTTCCCCGCCACCGGCCCGGGCTCCAGCGATGACGA  
GGACGACGACGAGGACGAGCACGGTGGCGTCTTCTCCAGTCCTTCCTGCCTGCTTCAGA  
TTCTGAAAGTGATATTATCTTTGACAATGAAGATGAGAACAGTAAAAGTCAGAATCAGGA  
TGAAGATTGCAATGAAAAGAATGGCTGCCATGAAAGTGAGCCATCAGTGACGACTGAGGC  
TGTGCACTACCTATACATCCAGATGGAGTACTGTGAGAAGAGCACTTTACGAGACACCAT  
TGACCAGGGACTGTATCGAGACACCGTCAGACTCTGGAGGCTTTTTTCGAGAGATTCTGGA  
TGGATTAGCTTATATCCATGAGAAAGGAATGATTACCGGGATTTGAAGCCTGTCAACAT  
TTTTTTGGATTCTGATGACCATGTGAAAATAGGTGATTTTGGTTTGGCGACAGACCATCT  
AGCCTTTTCTGCTGACAGCAAACAAGACGATCAGACAGGAGACTTGATTAAGTCAGACCC  
TTCAGGTCACTTAACCTGGGATGGTTGGCACTGCTCTCTATGTAAGCCAGAGGTCCAAGG  
AAGCACCAATCTGCATACAACCAGAAAAGTGGATCTCTTCAGCCTGGGAATTATCTTCTT  
TGAGATGTCCTATCACCCCATGGTCACGGCTTCAGAAAGGATCTTTGTTCTCAACCAACT  
CAGAGATCCCCTTCGCCTAAGTTTCCAGAAGACTTTGACGATGGAGAGCATGCAAAGCA  
GAAATCAGTCATCTCCTGGCTGTTGAACCACGATCCAGCAAACGGCCACAGCCACAGA  
GCTGCTCAAGAGTGAGCTGCTGCCCCACCCAGATGGAGGAGTCAGAGCTGCATGAAGT  
GCTGCACCACACGCTGACCAACGTGGATGGGAAGGCCCTACCGCACCATGATGGCCAGAT  
CTTCTCGCAGCGCATCTCCCCTGCCATCGATTACACCTATGACAGCGACATACTGAAGGG  
CAACTTCTCAATCCGTACAGCCAAGATGCAGCAGCATGTGTGTGAAACCATCATCCGCAT  
CTTTAAAGACATGGAGCTGTTTCAAGTGTGTACTCCACTACTGCTTCCCCGAAACAGACA  
AATATATGAGCACAACGAAGCTGCCCTATTTCATGGACCACAGCGGGATGCTGGTGATGCT  
TCCTTTTGACCTGCGGATCCCTTTTGCAAGATATGTGGCAAGAAATAATATATTGAATTT  
AAAACGATACTGCATAGAACGTGTGTTCAGGCCGCGCAAGTTAGATCGATTTTCATCCCAA  
AGAAGTTCTGGAGTGTGCATTTGATATTGTCACTTCTACCACCAACAGCTTTTCTGCCCCAC  
TGCTGAAATTATCTACACTATCTATGAAATCATCCAAGAGTTTCCAGCACTTCAGGAAAG  
AAATTACAGTATTTATTTGAACCATAACCATGTTATTGAAAGCAATACTCTTACACTGTGG  
GATCCCAGAAAGATAAACTCAGTCAAGTCTACATTATTCTGTATGATGCTGTGACAGAGAA  
GCTGACGAGGAGAGAAGTGGAAGCTAAATTTTGTAACTCTGTCTTTGTCTTCTAATAGTCT  
GTGTGCACTCTACAAGTTTATTGAACAGAAGGGAGATTTGCAAGATCTTATGCCAACAAT  
AAATTCAATTAATAAAACAGAAAACAGGTATTGCACAGTTGGTGAAGTATGGCTTAAAAGA  
CCTAGAGGAGGTTGTTGGACTGTTGAAGAACTCGGCATCAAGTTACAGGTCTTGATCAA  
TTTGGGCTTGTTTACAAGGTGCAGCAGCACAATGGAATCATCTTCCAGTTTGTGGCTTT  
CATCAAACGAAGGCAAAGGGCTGTACCTGAAATCCTCGCAGCTGGAGGCAGATATGACCT  
GCTGATTCCCCAGTTTAGAGGGCCACAAGCTCTGGGGCCAGTTCCCACTGCCATTGGGGT  
CAGCATAGCTATAGACAAGATATCTGCTGCTGTCTCAACATGGAGGAATCTGTTACAAT  
AAGCTCTTGACCTCCTGGTTGTAAGTGTGTCAGATGTCTATGTCCAGGGCCATCAA  
CCTAACCAGAACTCTGGACAGCAGGCATCACAGCAGAAATCATGTACGACTGGTCACA  
GTCCCAAGAGGAATTACAAGAGTACTGCAGACATCATGAAATCACCTATGTGGCCCTTGT  
CTCGGATAAAGAAGGAAGCCATGTCAAGGTTAAGTCTTTCGAGAAGGAAAGGCAGACAGA  
GAAGCGTGTGCTGGAGACTGAACTTGTGGACCATGTACTGCAGAACTGAGGACTAAAGT  
CACTGATGAAAGGAATGGCAGAGAAGCTTCCGATAATCTTGCAAGTGCAAAATCTGAAGGG  
GTCATTTTCTAATGCTTCAGGTTTGTGTTGAAATCCATGGAGCAACAGTGGTTCCCATTGT  
GAGTGTGCTAGCCCCGAGAAGCTGTGAGCCAGCACTAGGAGGCGCTATGAAACTCAGGT  
ACAACTCGACTTCAGACCTCCCTTGCCAACTTACATCAGAAAAGCAGTGAAATTGAAAT  
TCTGGCTGTGGATCTACCCAAAGAAACAATATTACAGTTTTTATCATTAGAGTGGGATGC  
TGATGAACAGGCATTTAACACAACCTGTGAAGCAGCTGCTGTACGCCTGCCAAAGCAAAG  
ATACCTCAAATTAGTCTGTGATGAAATTTATAACATCAAAGTAGAAAAAAGGTGTCTGT  
GCTATTTCTGTACAGCTATAGAGATGACTACTACAGAATCTTATTTTAACCCTAAAGAAC  
TGTCGTTAACCTCATTCAAACAGACAGAGGCTTATACTGGAATAATGGAATGTTGTACAT

## FIGURE 2HHH

TCATCATAATTTAAAATTAAATTCTAAGAAGAGGCTGGGTGCAGTGGCTCACACCTTTAA  
TCCCAGCACTTTGGGAAGCCAAGGCAGGAAGACTGCTTGAAACCAGGAGTTTGAGACCAG  
CCT

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ATGCTGGGGGGCAACTCCGGGGTCCGCAAGCGCAAGAGGAGGGCGACGGGGCTGGGGCT  
GTGGCTGCGCCGCCGGCCATCGACTTTCCCGCCGAGGGCCCGGACCCCGAATATGACGAA  
TCTGATGTTCCAGCAGAAATCCAGGTGTTAAAAGAACCCCTACAACAGCCAACCTTCCCT  
TTTGAGTTGCAAACCAACTCTTGCTGGTTTCTTTGCTGGAGCACTTGAGCCACGTGCAT  
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ATGGGGCTGTTGTCTTCTTCACTTGTAGTGACGAGTTTAGCTCATTGAGACTACATCAC  
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AAGGGTGCAACTAAAACAGTTTGCATGAAGGTCTACGGGAAGTGAAGGTGCTGGCAGGT  
CTTCAGCACCCCAATATTGTTGGCTATCACACCGCGTGGATAGAACATGTTTCATGTGATT  
CAGCCACGAGCAGACAGAGCTGCCATTGAGTTGCCATCTCTGGAAGTGCTCTCCGACCAG  
GAAGAGGACAGAGAGCAATGTGGTGTTAAAAATGATGAAAGTAGCAGCTCATCCATTATC  
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AATAACAAGTCGGTGAAGTACACCACCAATTTAGTCATAAGAGAATCTGGTGAAGTTGAG  
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TCTTCCGAAGAAAATGTCAACTTTTTTGGGTGAGACAGAGGCACAGTACCACCTGATGCTG  
CACATCCAGATGCAGCTGTGTGAGCTCTCGCTGTGGGATTGGATAGTCGAGAGAAACAAG  
CGGGGCCGGGAGTATGTGGACGAGTCTGCCTGTCTTATGTTATGGCCAATGTTGCAACA  
AAAATTTTTCAAGAATTGGTAGAAGGTGTGTTTTACATACATAACATGGGAATTGTGCAC  
CGAGATCTGAAGCCAAGAAATATTTTTCTTCATGGCCCTGATCAGCAAGTAAAAATAGGA  
GACTTTGGTCTGGCCTGCACAGACATCCTACAGAAGAACACAGACTGGACCAACAGAAAC  
GGGAAGAGAACACCAACACATACGTCCAGAGTGGGTACTTGTCTGTACGCTTCACCCGAA  
CAGTTGGAAGGATCTGAGTATGATGCCAAGTCAGATATGTACAGCTTGGGTGTGGTCTG  
CTAGAGCTCTTTCAGCCGTTTGGAACAGAAATGGAGCGAGCAGAAGTTCTAACAGGTTTA  
AGAACTGGTCAGTTGCCGGAATCCCTCCGTAAAAGGTGTCCAGTGCAAGCCAAGTATATC  
CAGCACTTAACGAGAAGGAACATCGCAGAGACCATCTGCCATTGAGCTGCTGCAGAGT  
GAACTTTTCCAAAATTCTGGAAATGTTAACCTCACCTACAGATGAAGATAATAGAGCAA  
GAAAAAGAAATTGCAGAACTAAAGAAGCAGCTAAACCTCCTTTCTCAAGACAAAGGGGTG  
AGGGATGACGGAAGGATGGGGGCGTGGGATGA

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CACAAGAGCCCTTCCTGCAGGGAACCTCAGGCTTCAGAGAGCCGAAAAGTTGGGAGGCGT  
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GGATTGCCGAAGAAGTCCAGGATTTCCGAAGCGAGCCGAAGCATCGCGACAGTTTTCAG  
AGACAGCTGATCGGTTGGAGCTGTTGCGCCGAGCAGTCATGGCGGCGGCCAGAGCTACTA  
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GGAGCAGCCGCTTCTTGAGCGGCCTGGAGCTGGTGAAGCAGGGTGCCGAGGCGCGCGTGT  
TCCGTGGCCGCTTCCAGGGCCGCGCGGCGGTGATCAAGCACCGCTTCCCCAAGGGCTACC  
GGCACCCGGCGCTGGAGGCGCGGCTTGGCAGACGGCGGACGGTGCAGGAGGCCCCGGGCGC  
TCCTCCGCTGTGCGCGCTGGAATATCTGCCCCAGTTGTCTTTTTTGTGGACTATGCTT  
CCAAGTGCTTATATATGGAAGAAATTGAAGGCTCAGTGAAGTTCGAGATTATATTCAGT  
CCACTATGGAGACTGAAAAAACTCCCCAGGGTCTCTCCAAGTATAGCCAAGACAATTGGGC

## FIGURE 2III

AGGTTTTGGCTCGAATGCACGATGAAGACCTCATTGATGGTGATCTCACCACCTCCAACA  
TGCTCCTGAAACCCCCCTGGAACAGCTGAACATTGTGCTCATAGACTTTGGGCTGAGTT  
TCATTTACAGCACTCCAGAGGATAAGGGAGTAGACCTCTATGTCCTGGAGAAGGCCTTCC  
TCAGTACCCATCCCAACACTGAACTGTGTTTTGAAGCCTTTCTGAAGAGCTACTCCACCT  
CCTCCAAAAGGCCAGGCCAGTGCTAAAAAATTAGATGAAGTGCGCCTGAGAGGAAGAA  
AGAGGTCCATGGTTGGGTAGAAGAATGTGTATGACAACCACACACAGTGAAGCTCTTTTT  
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ATGTGTCTAAGTCATGTTCTAGGCAGAATTGGGTATTTAAAGTAAATTGAGGACAGGCTT  
CTCCCAGATTGTGACATGTATATCTCAGATACATGGGTGTGGCATTGAACCACATAATGA  
GAACATTATTCTTTTTTAGTCCTTGTGAGACAAGGATGAAGTCTCAGTTGCTGATACTC  
GCTGAGCTTACTGGCCCTCTAACCAGTGTTTTTTTTTTGTTGTTGTTGTGTACATGTTAT  
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CAGCATGGAAAATATCAGTGTATTGTTTTATGAACTTTTACGTGTATATATAGACCAAG  
GATATGTGCTGAGTTTTGATGTCAAATATATTTCTCTTTCAGGGTCATGATCAAAAATG  
AAAAGTCTGCTTAACTCCAATTTCTCTTTTTAAAAAGCAGACTTACAGCTTTCAGGCAAC  
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GCTAGCTTTTAACTTGGCCAGCCTCAGTTTCTTTCTTAGAAGAAGCTATGTTTGGGTG  
GGAAGGGAAGAGAGGGGATAAGAAAATACCTTTCTTCTTGTAACTCCAATCAACAAACA  
TATTTTGAGTGCCTTTTGTGTTCCCTTGGCACCTGTTGGGTATTGGGTACTTGGCACCT  
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TGATTGCTACAGCTGAGCTAATTAACACCCATCACCTCACATAGTTACTGTCTTGTCTT  
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TGATTTCTTCTTTGACCCCTTGATTGTTTAGAAATCTGTTAATTTCCACACATTTGTAAA  
TGTTCCAATTTTTCTTTTGTATTGTCAGCTTCATTCCATTGTGTTTACAGATGATACAG  
TCAGTGCCTGTTCTTATGAAGCAAACTTCTATAATAGTAGGACCAGTACCCTGTCTGTT  
TCATTCACCACAGTCAGCATGCCCCAAGTGCCAGCATGGGGCGGATGGCCAGGAATGAG  
TGAAAACCTCCCTTCTGGGTAGTTGTGACTAGTAGAGAGGAAAAATAATATAATTGCCT  
GCTTACTGCATGCCAGGCATTGGGCTGGGAATTTTTATATTGGATCTAAAATAACTCTTA  
AGTTAGGCATTATCCCCATTTTATAGATGGAGAACTGGCCCCAAAAGGTGGGAACCTGT  
CCAAGACGTCACAGGTAGCAAGAGGTACTTTTACCTGGCTCCAAATCTGTGTTCTTTCCA  
CTGACAAATGAGATATGGGATATGGTGCATCTTTACAGTACTATAATAAGTATTGGCGTA  
TAACATTATTTTCAAGGAACTCCAAGGGCCACAGGAGCTGACAGGTTTTTCAATTAATAT  
TCCCAACATGAATGAGATGCCTCATTCCTCAGTTTCTCACGTGTACTATAAGGCTAGTA  
CCTGCTTTGTTGGGGTATGGTTGGCTCGTGTGCATTAAGTCAACAAATCCCTAGT

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CTGGTGCAGCAGGGCGCCGAGGCGCGCGTTTTCCGTGGCCGCTTCCAGGGCCGCGCGGCC  
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CGTCGGCGGACGGTGCAGGAGGCGCGCGCGCTGCTCCGCTGCCGCCGTGCGGGGATAGCT  
GCCCCAGTCGTCTTCTTTGTGGACTATGCGTCTAACTGCTTATATATGGAAGAAATCGAA  
GACTCGGTGACTGTTTCGGGATTATATCCAATCCACTATGGAGACTGAAAAGGACCCCCAG  
TGCTCTTGGACCTGGCCAGGAGGATGGGGCAGGTTCTGGCCGGAATGCACGACCAAGAC  
CTCATTACGGGGACCTCACACCTCCAACATGCTCCTGAGGCGGCCCTGGCGCAGCTG  
CACATCGTGCTCATCGACTTTGGGCTGAGCTTTGTCTCAGGACTGCCGGAAGATAAAGGC



## FIGURE 2JJJ

GTGACCTCTATGTCCTGGAGAAGGCCTTCCTCAGCACGCACCCCCACACCGAGACCGCG  
TTTGAAGCCTTTCTGAAGAGTTACGGGGCCTCGTCCAAGAAGTCCAGTCCAGTGCTGAAG  
AAGTTAGATGAGGTGCGCCTGAGAGGGCGAAAGCGGTCCATGGTCGGGTAGTGGAGCTGT  
GGTGAAGTGGCTCACGGTGAAGGATGATGTAGACGAGGCTGGACCCCTCAGCAAAGCATG  
GGTTGTTAAGTGGTCTGTGATCGTGCTGGGCCACCACCATCCATGGCTCACTGTTCTCAG  
GGGCTTCATGTACATGAGGTTTATTCTGGGCAGAACTGGGTAGGTAGCCCAGGCTAGCCT  
TGAATTTATGGCAACATCCTACCTCAGCTTGCTTGGAAGAGGTTATAAGCCACCATACCT  
GACTTTGCACTGATTCTGTCAGAAAC

SEQ ID NO: 76\_17000139801197\_H, IRAKM\_H  
ATGGCGGGGAACTGTGGGGCCCGCGCGCTGTCGGCGCACACGCTGCTGTTGACCTG  
CCGCCCCGCGCTGCTCGGAGAGCTCTGCGCTGTTCTGGACAGCTGCGACGGCGCGCTGGGC  
TGGCGCGGCCTGGCAGAGAGACTTTCAAGCAGCTGGCTGGATGTTTCGTATATTGAAAAG  
TATGTAGACCAAGGTAAAAGTGGAAACAAGAGAATTACTTTGGTCCTGGGCACAGAAAAAC  
AAGACCATCGGTGACCTTTTACAGGTCCTCCAGGAGATGGGACATCGTCGAGCTATTTCAT  
TTAATTACAACTATGGAGCAGTGTTGAGTCCTTCAGAGAAGAGTTATCAGGAAGGTGGA  
TTTCCAAATATATTATTCAAGGAAACAGCCAATGTACCCGTGGATAATGTTCTTATTCT  
GAACATAATGAAAAGGAGTACTGCTTAAATCTTCCATCAGCTTTCAAATATCATAGAA  
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AGAGTGGAGATTCAAACCTAACATATGCTGTCAAATTATTTAAACAGGAGAAAAAATG  
CAGTGTAAGAAGCATTGGAAGAGGTTTTATCTGAGCTTGAAGTTTTACTACTGTTTCAT  
CACCCAAACATACTAGAGTTGGCTGCATATTTTACAGAGACTGAGAAGTTCTGTCTGATT  
TATCCATACATGAGAAATGGAACACTTTTTTGACAGATTGCAGTGTGTAGGTGACACGGCC  
CCTCTCCCTTGGCACATTTCGAATCGGTATATTAATAGGAATATCCAAAGCCATTCACTAC  
CTGCACAACGTTCAACCATGCTCGGTATCTGTGGCAGTATATCAAGTGCAAACATCCTT  
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ATGCCAGAAGAGTACATCAGACAGGGGAACTTTCCATTAAAACAGATGTCTACAGCTTT  
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TCATTTCTAGATAAGAAAGTGCCTCCCTGCCCTCGGAATTTCTCTGCCAAGCTCTTCTGT  
TTGGCAGGCCGGTGTGCTGCAACGCGGGCAAAGTTAAGACCATCAATGGATGAAGTTTTA  
AATACTCTTGAAAGTACTCAAGCCAGCTTGTATTTTGTGTAAGATCCTCCCACATCACTA  
AAGTCCTTCAGGTGTCCTTCTCCTCTATTCCTGGAGAATGTACCAAGTATTCCAGTGGAA  
GATGATGAAAGCCAGAATAACAATTTACTACCTTCTGATGAAGGCCTGAGGATAGACAGA  
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AAAAAGCCAGAGAGCAAGAGAAATGAGGAAGCTTGCAACATGCCAGTTCCTTCTGTGAA  
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ATGTGGAAGAGATTTTTATCAGAACTGGAAGTTCTACTCCTGTTCCGTCACCCCCACATA  
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CACGTTGCAATCAGCGTATTGATAGGAATAGCCAAAGCCATCCAATACTTGACAAACACT  
CAGCCGTGCGCCGTATCTGTGGCAACGTTTCCAGTGCAAACATACTCTTGGATGACCAG  
CTCCAACCCAACTAACGGATTTTGTCTGCAGCGCACTTCCGACCCAATCTAGAGCAGCAG  
AGTTCTACCATAAATATGACCGGCGGTGGCAGGAAACATCTGTGGTACATGCCAGAAGAA



## FIGURE 2KKK

TACATCAGACAGGGAAGACTTTCCGTTAAAACTGATGTCTACAGCTTCGGAATCGTGATC  
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GACCTCCTCATGGAAGTGTGGAGAAAAGAGGCCTAGACTCCTGCCTGTCCTTCTTAGAC  
AGGAAGATACCACCCTGTCCTCGGAACCTTCTCTGCAAAGCTCTTCTCTCTGGCGGGCCGG  
TGTGTGGCAACGAAGGCCAAGTTAAGACCCACGATGGACGAAGTCCTGTCTCTCTGGAG  
AGCACCAGCCTAGCTTGTATTTTGCAGAAGACCCTCCCACGTCCTTGAAGTCCTTCAGG  
TGTCTTCTCCACTGTTCTTGGATAATGTCCCAAGTATTCCAGTAGAAGATGATGAAAAAC  
CAGAATAACCATTCAGTACCTCCCAAGGAAGTTTGGGGACAGATAGAGTGACTCAGAAA  
ACCCCTTTGAATGCAGCCAGTCTGAGGTACCTTTCTAGGCTTGGACCGAAACAGAGGG  
AACAGGGGAAGTGAAGCGGATTGCAACGTGCCAGTTCTTCTCATGAGGAATGCTGGTCC  
CCAGAGCTTGTGGCGCCATCCCAGGACTTAAGTCCTACTGTGATCAGTTGGGCTCGTCT  
TGGGAAGTACCAGGCCATTCTTATGGGAGCAAGCCAATGGAGAAGAGGTGTTCTCTGGG  
CTCTTTTGCAGTGAGCATGAACAGTCCAAAAAGCAGTGAATCCACCAGAAGATCAAGCAA  
AAAATAAAAGCAAACGTCACTGAAGGCACTGAGCAAATAGCATCCCCGTGAAAAGACAG  
AGCTCTGAGCTCCGTGAGTACAGCCAAGGGACCAACTGATGGAGAATTTGAATGGTGCAG  
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TCAAGTGACCGCCTCTCAGTCAAACCTGAGAAGCTAAACTGGAGCCAATCAGAATTATCC  
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GCAGCCAGTAGTCACCAGCAGCCAATCATGATACAGTGTCACTCTCCCTCTGCGCATGCC  
CTACGTCCTTTATAAAACCCAGGTCTTCAGGGCCACCCCTTCTTTTTTCCATCCTTGCT  
CAGAGGCAGCCTTTTGTATACATTCCCTGACCCCAACCCCAATTATATCTCTCATATGATA  
TCTGTTGCGTAGTGTGACTTTGTGGCATGACTTGGTTGTCAGATCATTGTCACAAGAACA  
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TGCTAGGGATACTGACAGTCTATTGCTTCCCATGGTTCATAGGGAAGTTGCTCAAATGCA  
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TTTTACAGCCAGTTGCTACTCTTGTGTTATCGCTGGTTAACCGGTCTGTCCGGAAGTGAGC  
CAAGTCATCCTTGCTAGGGCTTTTTCTGTGTAGAGAGGGAATTCCAGTCCAAAGTCTGCT  
TCTCTGTATTTAAATTCTTAGAAGAGTTGCCTGTGGCATTCCAATTGTTATATAAAAAA  
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ATGGCGAGTGCGGTGAGGGGTCGAGGCCGTGGCCCCGGCTGGGGCTCCAGCTCCAGTTC  
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GGCCACATCCGACTGCCTGCCTCAGGCCCCCGGGACACAGCCACCCTCTTCTACCTTG  
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AAAGCACTGGTCCACACAGGAGTGGCCCTGGTGCCTCGTGGACTGACCTGGCCCCCGCA  
GATGGCCCCACCACAGATGAGGTGACACTCCAAGTCTCAGGAGAGCGAGAGGGCTCACCC

## FIGURE 2LLL

AGCACTGCTGTTAGATACCCCTCAGGCAGTGTGGCCCTCCCAAGCCAGTGGCTGCTCATT  
GGACACCACGAGCTACCCCCAGTCCTGCACACCACCATGCTGAGGGTCCATCCCACCCTG  
GGGAGTGGAAGTGCAGAGACAAGACCTCCAGAGAATACCCAGGCCCCAGCCTTCTTCTTG  
GAGCTATTGAGCCTGAGCCGAGAGAACTTTGGGACTCCGAGCTGCATCCAGAAGAAAA  
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GTCCTCCTGGGAGGGTGGATTCTCTTTGTGATGAGGCAGGTGGTGGAGAAGCAGCAGGAG  
ACCCCCCTGGCACCTGCAGACTTTGCTCACATCTCCCAGGATGCCCAGTCCCTGCACTCG  
GGGGCCAGCCGGAGGAGCCAGAAGAGGCTTCAGAGTCCCTCAAAGCAAGCCCAGCCACTC  
GACGACCCTGAAGCTGAGCAACTCACCGTAGTGGGGAAGATTTCTTTCAATCCCAAGGAC  
GTGCTGGGCCGCGGGGAGGCGGGACTTTCTGTTTTCCGGGGACAGTTTGAGGGACGGGCA  
GTGGCTGTCAAGCGGCTCCTCCGCGAGTGCTTTGGCCTGGTTCGGCGGGAAGTTCAACTG  
CTGCAGGAGTCTGACAGGCACCCCAACGTGCTCCGCTACTTCTGCACCGAGCGGGGACCC  
CAGTTCCACTACATTGCCCTGGAGCTCTGCCGGGCTCCTTGCCAGGAGTACGTAGAAAAC  
CCGGACCTGGATCGCGGGGGTCTGGAGCCCCGAGGTCTGCTGCAGCAGCTGATGTCTGGC  
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GAGGAAGAGGTCCACGACAAGGTGGTTGCCCGGACCTGGTTGGAGCCATGTTGAGCCCA  
CTGCCGAGCCACGCCCCCTCTGCCCCCAGGTGCTGGCCCCACCCCTTCTTTTGGAGCAGA  
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GGAGGGTTGCAATTGCAACGGCAGCTGCCGGGCGTATGTGTTGGTGCTAGAGGCAGCTGC  
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GACTTTTATCGATTCCACACATTAATCTTTCAAATGATGATGATGAAGATAAACTTT  
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## FIGURE 2MMM

TAATGAAGACCCTAAAGATCGTCCTTCTGCTGCACACATTGTTGAAGCTCTGGAAACAGA  
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TTTTGCTGATGTGTTTATCAAATGATAACTGGAAGCTGAGGAGAATATGCCTCAAAAAGA  
GTAGCTCCTTGGATACTTCAGACTCTGGTTACAGATTGTCTTGATCTCTTGGATCTCCTC  
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ATCTCCAAGAGGGTTGTCTCATTCTCCTTGGGCCGTGAAAAAGATAAGTCTTTTATGCGA  
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SEQ ID NO: 81\_5R57\_10\_2\_M TESK2\_M

GCTGCTGGACAGTGACTTGTATTTACCGTGGACTGTGAGAGTGAACTGGCCTATGGCAT  
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GGTGTGAAGGCTTTGCTTTC

SEQ ID NO: 82\_AA232253\_H

ATGTCGTCTCTCGGTGCCTCCTTTGTGCAAATTAAATTTGATGACTTGCAGTTTTTTTGAA  
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AGTCACAGAAACATCATCCAGTTTTATGGAGTAATTCTTGAACCTCCCAACTATGGCATT  
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GAGATGGATATGGATCACATTATGACCTGGGCCACTGATGTAGCCAAAGGAATGCATTAT  
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## FIGURE 2NNN

ATAGCTGCTGATGGAGTATTGAAGATCTGTGACTTTGGTGCCTCTCGGTTCATAACCAT  
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AGCAAAGTCAGCGAAGGGGGCTGGACAAAAGTGGAATACCGGAAAAAGCCCCACAGGCCA  
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TGA

SEQ ID NO: 83\_AI375137\_H

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GAAGAAGGCAGCAAAGCAGATGTGAATGCTCAAGATAATGAAGACCATGTCCCACTCCAT  
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## FIGURE 2000

GGCAAATTTGAAGTTGCCAAGGAAATCATCCAAATATCAGGAACAGAAAGTCTGACTAAG  
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CACACTGGATTACACTCTGCTTGCTACCACGGTCACATTTCGCCTGGTTTCTTACTG  
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CAGTCTAAATTAATTATTGCAGTAGATGTTGCCAAAGGCATGGAGTACCTTCACAACCTG  
ACACAGCCAATTATACATCGTGACTTGAACAGTCACAATATTCTTCTCTATGAGGATGGG  
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GGGTGGAACGCATGTCTGAAGGAAGACCCGAATTTTCTGAAGTTGTCATGAAGTTAGAA  
GAGTGTCTCTGCAACATTGAGCTGATGTCTCCTGCATCAAGTAACAGCAGTGGGTCTCTC  
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TTGTCCCAAAGTGCTGGACAATATTCCCTCTCAAGGTCTGTCTTTGGAGGAGATGAAAAGA  
AGTCTTCAATACACACCCATTGACAAATATGGCTATGTATCCGATCCCATGAGCTCAATG  
CATTTTCATTCTTGCCGAAATAGTAGCAGCTTTGAGGACAGCAGCTGA

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GCTTTATCGCCAGCTAATTGACCTGGGCTATCTGAGCAGCAGTCACTGGAACTGTGGGGC  
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CTTGAGCACATTTTCTCACCAGGTGTTACAGACTCGCCTGGTGGATGCAGCCAAGGCCCT  
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TAAGAGCATTTCAGCCAATTCCGGACTCGGCTCAATAGTTCCACGAGGCTTTTGCAGC  
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## FIGURE 2PPP

TTTACAGGATGTCTTGCTTCATCGTAAACCTAAACTGGGACAGGAAGTGGGCCGGGGCCA  
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AGTTGTCCCTCCAGATGAGAAGCACTGGAATGATCTGGCTTTGGAATTTCACTATATGAG  
GTCTCTGCCGAAGCATGAGCGATTGGTGGATCTCCATGGTTCAGTCATTGACTACAATA  
TGGTGGTGGCTCCAGCATTGCTGTGCTCCTCATTATGGAGCGGCTACACCGGGATCTCTA  
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CTCAGGCTCTGTCAAGCTCCCTGAGGCATTTGAGAGGTGTGCTAGCAAAGACCATCTCTG  
GAACAATGTGCGGAGGGGGGCTCGCCCAGAACGCTTCTCTGTGTTTGATGAGGAGTGCTG  
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CCAGCCCATGCTCCAGGGCATCATGAATCGGCTCTGCAAGTCCAATTCTGAGCAGCCAAA  
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CTCCCAAGGGAAGTGGTGTCTGCTGGGAACTTGGAACTTCCCAGGCAGGGATGACTCC  
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SEQ ID NO: 85\_W20810\_M

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CACCGGCTCTCGTCTTCAACAAGTCTTGAAGTGCAGATTGGGAACTACAACCTCCTTGG  
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SEQ ID NO: 86\_AA744236\_H

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## FIGURE 2QQQ

CAGTCAATAAGAGACCCAGCATCTATCCCTCCTGAAGAGATGTCTCCAGAATTCACAAC  
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GTGCTTCTCCAGTTGTTTGAAGTTCATGAAGAGCATGTGCGGATGGTGTGCTGTCTCAC  
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SEQ ID NO: 87\_AI052250\_H

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## FIGURE 2RRR

TGCCCCAGCGTGTCATTGTGCAGAGAATTTGCCTTGTTTGACTTCAGAATTTGTAAACC  
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TCCAGATTTTGTAAATTTTCCTACAAAAATGGATTGTCTACTAACC AAAACCCCTCCTG  
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CCATGAAAAACGCTTTGATACCAAGAATTA AAAATGCTTGCTACAAACATCTTCCCTTG  
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SEQ ID NO: 88\_AA278842\_H  
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CCAAATCCCCAGAGTCCGACTGGAGCAGCTGGGAAGCTGAGGGCTCCTGGGAACAGGGTT  
GGCAGGAGCCAAGCTCCCAGGAGCCACCTCCTGACGGTACACGGCTGGCCAGCGAGTATA  
ACTGGGGTGGCCCAGAGTCCAGCGACAAGGGCGACCCCTTCGCTACCTGTCTGCACGTC  
CCAGCACCCAGCCGAGGCCAGACTCTTGGGGTGAAGCAACTGGGAGGGCCTCGAGACTG



## FIGURE 2SSS

ACAGTCGACAGGTCAAGGCTGAGCTGGCCCCGAAGAAGCGCGAGGAGCGGCGGGCGGGAGA  
TGGAGGCCAAACGCGCCGAGAGGAAGGTGGCCAAGGGCCCCATGAAGCTGGGAGCCCCGGA  
AGCTGGACTGAACCGTGGCGGTGGCCCTTCCCCGCTGCGGAGAGCCCGCCCCACAGATGT  
ATTTATTGTACAAACCATGTGAGCCCGGCGCCAGCCAGGCCATCTCACGTGTACATA  
ATCAGAGCCACAATAAATTCTATTTTAC

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ATGGCCTTCATGGAGAAGCCGCCAGCCGGCAAGGTGCTGCTGGACGACACGGTGCCGCTG  
ACAGCAGCCATCGAGGCGAGCCAGAGCCTGCAGTCCCACACGGAATATATTATTCGAGTG  
CAAGGAGGAATTTCTGTGGAAAACAGCTGGCAGATTGTTAGAAGATACAGTGAATTTGAT  
TTGCTTAACAACAGCTTACAGATTGCAGGCCTAAGTCTACCTCTTCCTCCCAAAAATTG  
ATTGGTAACATGGATCGTGAATTCATAGCTGAAAGGCAGAAAGGTCTTCAGAACTATCTC  
AACGTGATCACAACAAATCATATCTTGTCTAATTGTGAGCTGGTTAAGAAGTTTTTAGAT  
CCAAACAACCTATTCCGCAAACATACTGAGATTGCCTTGCAACAGGTTTCCATGTTCTTC  
CGATCAGAGCCAAAGTGGGAGGTGGTGAACCTTTGAAAGACATAGGTTGGAGAATAAGG  
AAGAAATATTTCTTGATGAAGATTAAAAATCAGCCAAAGGAACGGCTAGTGTTAAGCTGG  
GCTGACCTTGGCCGAGACAAGTATTTGTGAGATAAAGATTTTCAGTGTCTAATCAAACCTT  
CTGCCTTCTTGTGTTGCACCCTTACATCTATCGGGTTACCTTTGCCACAGCTAATGAATCC  
TCAGCGTTGCTAATTAGGATGTTTAAAGAAAAGGGAACATTGAAGGATCTGATCTACAAG  
GCAAAACCAAAGACCCATTTCTAAAGAAGTACTGCAACCCTAAGAAGATTCAGGGCCTG  
GAACTCCAGCAAATAAAAACATATGGACGGCAAATATTAGAGGTACTGAAGTTTCTTCAT  
GACAAGGGATTCCCTTATGGGCATCTTCACGCCTCCAATGTGATGCTCGATGGGGACACT  
TGCCGGCTGCTGGACCTTGAGAATTCCTTATTGGGCCTGCCTTCCTTACCGATCTTAT  
TTTTTACAATTCAGGAAAATCAATACATTGGAAAGTGTGGATGTCCACTGCTTTGGCCAC  
TTACTGTATGAAATGACTTATGGACGACCGCCAGACTCGGTGCCTGTGGACTCCTTCCT  
CCTGCCCCGTCCATGGCTGTGGTGGCCGTGTTGGAGTCTACGCTGTCTTGTGAAGCCTGT  
AAAAATGGCATGCCTACCATCTCCCGCTCTTACAGATGCCATTATTACGCGATGTTTTA  
CTAACCCTTCTGAAAAACACAGTTTAAAGATCCCTACAAAGTTAAAGAGGCATTGAGA  
ATTGCCAAAGAATGTATAGAGAAGAGACTAATTGAGGAACAGAAACAGATTCACCAGCAT  
CGAAGACTGACAAGAGCTCAGTCCCACCATGGATCTGAGGAGGAAAGAAAAAAGAAAG  
ATTTTAGCTCGAAAGAAGTCAAAACGATCTGCTCTTGAAAATAGTGAAGAGCATTACGG  
AAGTACAGCAACTCCAATAATTACGAGGATCTGGGGCCAGCTCACCTCTCACGTCCCCG  
TCATCGCCAACTCCACCCTCTACATCAGGGATATCTGCATTACCTCCACCTCCTCCACCT  
CCACCACCACAGCAGCTCCCTTGCCTCCTGCGAGCACCGAGGCACCTGCCAGCTCTCG  
TCTCAGGCTGTGAATGGCATGAGCCGAGGGGCTTGCTCAGCTCCATCCAGAATTTCCAA  
AAAGGAACCTTGAGGAAAGCCAAACCTGTGATCACAGTGCTCCGAAGATCGGCTGAAGCT  
TCCTGTTTACACTTGAGGGGAAAGTTCTTTTTTATTCTACTACCCCTACCCCCAAC  
TACCCTCTTCTGGGAAAGTAATTGCTGAGCCAGTACAGCCACAAACAGTACTATTTTGC  
AGATGCTCATGTAAGCAGCTTTTCGAGAGAAATAATTCTTTAAGCAGAATAAAGTTAGGC  
TGGCATGCAAAAAAAAAAAAAAAAAAAAAA

SEQ ID NO: 90\_AA425725\_H

ATGAGCGCCAGCACGGGCGGTGGTGGGGACAGCGGCGGCAGCGGCGGCAGTAGCAGCAGC  
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CCTCAGATGCTGCAGGGCCTTCTGGGCTCCGACGACGAGGAACAGGAAGACCCCAAGAC  
TACTGCAAGGGCGGCTACCACCCTGTGAAGATCGGCGACGTGTTCAATGGGCGGTACCAC  
GTGGTGCGCAAACTGGGCTGGGGCCACTTCTCCACCGTCTGGCTCTGCTGGGACATCCAG  
CGCAAGCGCTTTGTGGCCCTCAAAGTGGTGAAGAGTGCAGGGGATTACACGGAGACAGCT  
GTGGATGAGATCAAGCTCCTGAAATGTGTCCGGGACAGCGACCCCAAGTACCCCAAGGA  
GAGACCATTGTCCAGCTCATTGATGACTTCAGGATCTCAGGAGTCAATGGAGTCCATGTG

## FIGURE 2TTT

TGCATGGTGTCTGGAGGTGCTGGGCCACCAGCTCCTCAAATGGATCATCAAGTCCAACCTAC  
CAGGGCCTGCCCCGTGCCCTGCGTGAAGAGCATCGTGAGGCAGGTGCTGCACGGCCTGGAC  
TACCTCCACACCAAGTGCAAGATCATCCACACGGACATCAAGCCCCGAGAACATCTTGCTG  
TGTGTGGGGGACGCTTACATCAGGCGCCTGGCTGCCGAGGCCACGGAGTGCGCAACAGGCA  
GGGGCGCCGCCCCCTCCCGCTCCATAGTCAGCACTGCCCCCAGGAGGTCTTGACCGGT  
AAGCTGTCCAAAAACAAGAGGAAGAAGATGAGGCGCAAACGGAAACAGCAGAAGCGGCTG  
CTGGAGGAGCGGCTGCGGGACCTGCAGAGGCTGGAGGCCATGGAGGCTGCCACCCAGGCT  
GAGGACTCTGGCTTGAGACTAGACGGGGGCAGCGGCTCCACATCCTCTTCAGGCTTCTCC  
GGCTCCCTCTTCTCTCCTGCCTCCTGCTCCATCCTCTCCGGCTCGTCCAATCAGCGAGAG  
ACCGGGGGCCTCCTGTCGCCTAGCACACCATTGCGGTGCCTCGAACCTCCTGGTGAACCCC  
CTGGAGCCCCAAAATGCAGATAAGATCAAGATCAAGATCGCAGACCTGGGCAACGCCTGC  
TGGGTGCACAAGCACTTCACGGAAGACATCCAGACTCGGCAGTACCGGGCCGTCGAGGTG  
CTGATCGGCGCCGAATACGGCCCCCGGCAGACATCTGGAGCACAGCCTGCATGGCCTTC  
GAGCTGGCCACTGGTGACTACCTGTTTCGAGCCGCATTCTGGAGAAGACTACAGTCGTGAT  
GAGGACCACATCGCTCACATAGTGGAGCTTCTGGGGGACATCCCCCAGCCTTCGCCCTC  
TCAGGCCGCTATTCCCGGGAGTTCTTCAACCGGAGAGGAGAGCTGCGGCACATCCACAAT  
CTCAAGCACTGGGGCCTGTACGAGGTAATCATGGAAAAGTACGAGTGGCCCCCTAGAGCAG  
GCCACACAGTTTCAGCGCCTTTCTGCTGCCCCATGATGGAGTACATCCCCGAAAAGCGGGCC  
AGTGCCGCTGACTGCCTCCAGCACCCCTGGCTCAACCCCTAG

SEQ ID NO: 91\_SGK022\_H

TCTGGCCCTGTCCCTCCCCACCACCCGCCGCTGTGTCCAGACAGAGAATGTTCTAACGCT  
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GTAGAGCTGCCTCTCAGAGGCAGCATGAGCTGAGAGGGTGATAGGAAGGCGGCGCTAGAC  
AGCATGGAGGACTTTCTGCTCTCCAATGGGTACCAGCTGGGCAAGACCATTGGGGAAGGG  
ACCTACTCAAAAGTCAAAGAAGCATTTTCCAAAAAACACCAAAGAAAAGTGGCAATTAAA  
GTTATAGACAAGATGGGAGGGCCATCAGAGTTTATCCAGAGATTCTCCTCGGGAGCTC  
CAAATCGTCCGTACCCTGGACCACAAGAACATCATCCAGGTGTATGAGATGCTGGAGTCT  
GCCGACGGGAAAATCTGCCTGGTGATGGAGCTCGCTGAGGGAGGGGATGTCTTTGACTGC  
GTGCTGAATGGGGGGCCACTGCCTGAAAGCCGGGCCAAGGCCCTCTTCCGTGAGATGGTT  
GAGGCCATCCGCTACTGCCATGGCTGTGGTGTGGCCACCAGGACCTCAAATGTGAGAAC  
GCCTTGTTGCAGGGCTTCAACCTGAAGCTGACTGACTTTGGCTTTGCCAAGGTGTTGCC  
AAGTCACACCGGGAGCTGAGCCAGACCTTCTGCGGCAGTACAGCCTATGCTGCCCCCGAG  
GTGCTGCAGGGCATTCCCCACGATAGCAAAAAGGTGATGTCTGGAGCATGGGTGTGGTC  
CTGTATGTATGCTCTGTGCCAGCCTACCTTTTGACGACACAGACATCCCCAAGATGCTG  
TGGCAGCAGCAGAAGGGGGTGTCTTCCCCACTCATCTGAGCATCTCGGCCGATTGCCAG  
GACCTGCTCAAGAGGCTCCTGGAACCCGATATGATCCTCCGGCCTTCAATTGAAGAAGTT  
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GTAGGGGGAGAAAGCAAA

SEQ ID NO: 92\_AA060026\_M SGK022\_M

CAGACGGAGAATGTTCTAGCCCTGGAGGCAGCTGTGAATGAAGTCCTTGGGGGGAAAAGA  
AGCAGGCCCGAGGGCGATGGTGGAGTAGAGCTGCCTCGCAGAGGCAGCATGAGCTGAGAGG  
GTGACAAGAAGGAGGCGCTACACAGCATGGAGGACTTTCTACTCTCCAATGGGTATCAGC  
TGGGCAAGACCATTGGGGAAGGGACCTACTCAAAAGTCAAAGAAGCATTTTCCAAAAAAC  
ATCAAAGAAAAGTGGCAATTAAATATAGACAAGATGGGAGGGCCAGAAGAGTTTATCC  
AGAGATTCTGCTCGTGAGCTCCAGATTGTCCGTACCCTGGACCACAAAAACATCATCC  
AGGTGTATGAGATGCTGGAGTCAGCAGATGGAAAATCTACCTGGTGATGGAACTGGCTG  
AGGGAGGGGATGTCTTTGACTGTGTGCTGAACGGAGGGCCACTTCCCGAGAGCCGGGCCA  
AGGCCCTCTTCCGCCAGATGGTTGAGGCTATTGCTATTGCCATGGCTGTGGCGTGGCCC

## FIGURE 2UUU

ACCGGGACCTTAAGTGTGAGAACGCCTTGTTGCAGGGCTTCAACCTGAAGCTGACCGACT  
TTGGCTTTGCCAAGGTGCTACCCAAGTCACGCAGGGAGCTGAGCCAGACCTTCTGTGGCA  
GCACAGCCTATGCCGCCCTGAGGTGCTACAGGGCATACCCCATGATAGCAAGAAAGGTG  
ATGTCTGGAGCATGGGTGTGGTCCTGTATGTAATGCTCTGTGCAAGTCTACCTTTTGATG  
ACACAGATATCCCCAAGATGCTGTGGCAGCAGCAGAAGGGGGTGTCTTCCCCACTCATT  
TGGGCATCTCAACCGAATGCCAGGACCTGCTCAAGCGGCTCCTGGAACCAGACATGATAC  
TCCGGCCTTCAATCGAAGAAGTTAGTTGGCACCCATGGCTAGCAAGCACTTGATAAAAGC  
AATGGCAAGTCCTCCCCAATAAAGTAGGGGGAGAAAGCAAAGCTG

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CTCCCCAAGTGCTGGGATTACAGGCGTGAGCCACCGCGCCCGGCGCACTTCATTCTCAA  
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AGGAGTTCCGTAACCAAAAGGAGAAAGTAACAACAGCCAGTGGAGACAAAAGAAGTCTGCT  
TCTCTTTCTTTCCCCCTCCAAGTTCCTAGTGGAGGGCTGAGTCCAGCATCCCAGACTCGT  
GTGACTATATAGGCAAGCATTTGGGGACCTACTTCACTTTGATACCCTAGCCTTCAGCAG  
CTCAAGGTGTTGGCCTTTGGATAGGAGGCTTCCAAGTAGTAAAGCTCCCTGCTCTCAGCA  
AGCCCAACACCATGGGGAAGGGAGATGTCTTAGAGGCAGCACCAACCACACAGCCTACC  
ATTCCTCATGGATGAATATGGTTATGAGGTGGGCAAGGCCATTGGCCATGGCTCCTATG  
GGTCGGTATATGAGGCTTTCTACACAAAGCAGAAGGTTATGGTGGCAGTCAAGATCATCT  
CAAAGAAGAAGGCCTCTGATGACTATCTTAACAAGTTCTTGCCCCGTGAAATACAGGTAA  
TGAAAGTCTTGCGGCACAAGTACCTCATCAACTTCTATCGGGCCATTGAGAGCACATCTC  
GAGTATACATCATTCTGGAAGTGGCTCAGGGTGGTGTATGTCCTTGAATGGATCCAGCGCT  
ACGGGGCCTGCTCTGAGCCCCCTTGCTGGCAAGTGGTTCTCCCAGCTGACCCTGGGCATTG  
CCTACCTGCACAGCAAGAGCATCGTGCACCGGGACTTAAAGTTGGAGAACCTGTTGCTGG  
ACAAGTGGGAGAATGTGAAGATATCAGACTTTGGCTTTGCCAAGATGGTGCCTTCTAACC  
AGCCTGTGGGTGTAGCCCTKCTTACCGCCAAGTGAAGTGCCTTTTCCACCTCAGCCAGA  
CTTACTGTGGCAGCTTTGCTTACGCTTGCCAGAGATCTTACGAGGCTTGCCCTACAACC  
CTTTCCTGTCTGACACCTGGAGCATGGGCGTCATCCTTTACACTCTAGTGGTTCGCCCCATC  
TGCCCTTTGATGACACCAATCTCAAAAAGCTGCTAAGAGAGACTCAGAAGGAGGTCACTT  
TCCCAGCTAACCATACCATCTCCCAGGAGTGCAAGGTCCAAGTGCCTCATTGCCTGTGTGG  
CACAATGGAGAAAACTCAGGCAAGACCTCTCTCTCCCCTGCTCTAGAACCCTGATCCTCC  
AGATGCTACGCCAAGCCACTAAGCGTGCCACCATTCTGGACATCATCAAGGATTCTCTGGG  
TGCTCAAGTTCAGCCTGAGCAACCCACCCATGAGATCAGGCTGCTTGAGGGCCATGTGCC  
AGCTCCACAACACCACTAAACAGCACCAATCCTTGCAAATTACGACCTGAAAATGGCTGA  
GGGAGGGGGCTAAGAGAGGAGCAAAGCAGGAGGTCTTGGGCTAAAAATCTTTTTTACCAA  
AAATAAATCTAAGTCTGATTTAGTTTCATCAAAAAA

SEQ ID NO: 94\_AA758539\_H

GACCATTGACAGCGCTCCGGTAGTGTAATGAGGACAATGCCTGCTGGCCCCACATGACGG  
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AAGGAAGAAGGGTTACATCGTAGGCATCAATCTTGGCAAGGGTTCCTACGCAAAAGTCAA  
ATCTGCCTACTCTGAGCGCCTCAAGTTCAATGTGGCTGTCAAGATCATCGACCGCAGGAA  
AACACCTACTGACTTTGTGGAGAGATTCTTCTCGGGAGATGGACATCCTGGCAACTGT  
CAACCACGGCTCCATCATCAAGACTTACGAGATCTTTGAGACCTCTGACGGACGGATCTA  
CATCATCATGGAGCTTGGCGTCCAGGGCGACCTCCTCGAGTTCATCAAGTGCCAGGGAGC  
CCTGCATGAGGACGTGGCAGCAAGATGTTCCGACAGCTCTCCTCCGCCGTCAAGTACTG  
CCACGACCTGGACATCGTCCACCGGGACCTCAAGTGCGAGAACCTTCTCCTCGACAAGGA  
CTTCAACATCAAGCTGTCTGACTTTGGCTTCTCCAAGCGCTGCCTGCGGGACAGCAATGG  
GCGCATCATCCTCAGCAAGACCTTCTGCGGGTTCGGCAGCATATGCAGCCCCCGAGGTGCT  
GCAGAGCATCCCCTACCAGCCCAAGGTGTATGACATCTGGAGCCTGGGCGTGATCCTGTA

## FIGURE 2VVV

CATCATGGTCTGCGGCTCCATGCCCTATGACGACTCCGACATCAGGAAGATGCTGCGTAT  
CCAGAAGGAGCACCCTGTGGACTTCCCCGCGCTCCAAGAACCTGACCTGCGAGTGCAAGGA  
CCTCATCTACCGCATGCTGCAGCCCCGACGTGAGCCAGCGGCTCCACATCGATGAGATCCT  
CAGCCACTCGTGGCTGCAGCCCCCAAGCCCAAGCCACGTCTTCTGCCTCCTTCAAGAG  
GGAGGGGGAGGGCAAGTACCGCGCTGAGTGCAAACCTGGACACCAAGACAGGCTTGAGGCC  
CGACCACCGCCCCGACCACAAGCTTGGAGCCAAAACCCAGCACCAGGCTGCTGGTGGTGCC  
CGAGAACGAGAACAGGATGGAGGACAGGCTGGCCGAGACCTCCAGGGCCAAAGACCATCA  
CATCTCCGGAGCTGAGGTGGGGAAAGCAAGCACCTAGCATGACAATGGCCCCGTGTGTG  
TGGTGGGGGTCGGGGTTGGGGGCGATGGTGCAGTCGGCCTTCACGTAAACTAAGTAGGCA  
GGTAGGATCTGAAGAAGGCACAGGTGCAAGTAAATTCGTCAATTAAACCACTATTTTGA  
TT

SEQ ID NO: 95\_AA883975\_H  
ATGTCGGGAGACAACTTCTGAGCGAACTCGGTTATAAGCTGGGCCGCACAATTGGAGAG  
GGCAGCTACTCCAAGGTGAAGGTGGCCACATCCAAGAAGTACAAGGGTACCGTGGCCATC  
AAGGTGGTGGACCGGCGGAGCGCCCCGGACTTCGTCAACAAGTTCCTGCCGCGAGAG  
CTGTCCATCCTGCGGGGCGTGCGACACCCGCACATCGTGACGTCTTCGAGTTCATCGAG  
GTGTGCAACGGGAACTGTACATCGTGATGGAAGCGGCCGCCACCGACCTGCTGCAAGCC  
GTGCAGCGCAACGGGCGCATCCCCGGAGTTCAGGCGCGGACCTCTTTGCGCAGATCGCC  
GGCGCCGTGCGCTACCTGCACGATCATCACCTGGTGCACCGCGACCTCAAGTGCGAAAAC  
GTGCTGCTGAGCCCCGACGAGCGCCGCGTCAAGCTCACCGACTTCGGCTTCGGCCGCCAG  
GCCCATGGCTACCCAGACCTGAGCACCACCTACTGCGGCTCAGCCGCCTACGCGTCACCC  
GAGGTGCTCCTGGGCATCCCCTACGACCCCCAAGAAGTACGATGTGTGGAGCATGGGCGTC  
GTGCTCTACGTCATGGTCACCGGGTGCTGCCCTTCGACGACTCGGACATCGCCGGCCTG  
CCCCGGCGCCAGAAACGCGCGTGCTCTATCCCGAAGGCCTCGAGCTGTCCGAGCGCTGC  
AAGGCCCTGATCGCCGAGCTGCTGCAGTTCAGCCCCGTCCGCCAGGCCCTCCGCGGGCCAG  
GTAGCGCGCAACTGCTGGCTGCGCGCCGGGACTCCGGCTAG

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CTGGTAGAGAACAGGGGCTGGTGCCAAGGCCCATGGAGATGAGAAAACGGAAGACAGGGA  
TCATGGAAAGAATTGTGGGGTCAAGGGACAGTGGCGGGAGGAGCTGGCTCACCACCCTGT  
GGACAAATCAGGCCTTATAATTTGTGATTCTGTGGCTTTGTCTAAAAGTCCATAAAGCAC  
CTTGATATCCAGTCTCACAGACTGCTCACAACAGTCCACAAGGCTGGTGGGGAGTGCTTC  
TTTTGAATGATATACTAACGACAAAAATAATAGAAGTGAACATTCTTTGCAATGTCCAAG  
CAGCTAGACACACTTAAGACCATTAAGAAAGCCAAGAAATAAGACCCAGACAAGGTGGGC  
AGAAGTTGGAAGGCAGGAGACAGGTGTGAGGAGGTGGGCCTTTCTGATCTGCCAGCCCAT  
CTCTCCTCCCCTTACTTCCTCAGAGTTTATCCAGAGATTCTCCTCCCTCGGGAGCTCCAAAT  
CGTCCGTACCCTGGACCACAAGAACATCATCCAGGTGTATGAGATGCTGGAGTCTGCCGA  
CGGGAAAATCTGCCTGGTGATGGAGCTCGCTGAGGGAGGGGATGTCTTTGACTGCGTGCT  
GAATGGGGGGCCACTGCCTGAAAGCCGGGCCAAGGCCCTCTTCGTCAGATGGTTGAGGC  
CATCCGCTACTGCCATGGCTGTGGTGTGGCCACCGGGACCTCAAATGTGAGAACGCCTT  
GTTGCAGGGCTTCAACCTGAAGCTGACTGACTTTGGCTTTGCCAAGGTGTTGCCCAAGTC  
ACACCGGGAGCTGAGCCAGACCTTCTGCGGCAGTACAGCCTATGCTGCCCCCGAGGTGCT  
GCAGGGCATTCCCNCAAGATGCTGTGGCAGCAGCAGAAGGGGGTGTCTTCCCCACTCA  
TCTGAGCATCTCGGCCGATTGCCAGGACCTGCTCAAGAGGCTCCTGGAACCCGATATGAT  
CCTCCGGCCTTCAATTGAAGAAGTTAGTTGGCATCCATGGCTAGCAAGCACTTGATAAAA  
GCAATGGCAAGTGCTCTCCAATAAAGTAGGGGGAGAAAGCAAACCC

## FIGURE 2WWW

SEQ ID NO: 97\_H29974\_H  
TTACAGCCTGTTGGCGGAGATCGGGCGCGGCAGCTACGGCGTGGTTTATGAGGCAGTGGC  
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GGAGCTGGCGCTGGCTGAATTCTGGGCCCTCACCAGCCTCAAGCGGCGCCACCAGAACGT  
CGTGACGTTTGAGGAGTGCGTCCTGCAGCGCAATGGGTAGCCCAGCGCATGAGTCACGG  
CAACAAGAGCTCGCAGCTTTACCTGCGCCTGGTGGAGACCTCGCTGAAAGGAGAAAGGAT  
CCTGGGTTATGCTGAGGAGCCCTGCTATCTCTGGTTTGTCTGAGGTTCTGTGAAGGTGG  
AGACCTGAATCAGTATGTCCTGTCCCGGAGGCCAGACCCAGCCACCAACAAAAGTTTCAT  
GCTACAGCTGACGAGCGCCATTGCCTTCCTGCACAAAAACCATATTGTGCACAGGGACCT  
GAAGCCAGACAACATCCTCATCAGAGCGGTCTGGCACCCCCATCCTCAAAGTGGCCGA  
CTTTGGACTAAGCAAGGTCTGTGCTGGGCTGGCACCCCGAGGCAAAGAGGGCAATCAAGA  
CAACAAAAATGTGAATGTGAATAAGTACTGGCTGTCTCAGCCTGCGGTTTCGGACTTCTA  
CATGGCTCCTGAAGTCTGGGAGGGACACTACACAGCCAAGGCGGACATCTTTGCCCTGGG  
CATTATCATCTGGGCAATGATAGAAAGAATCACTTTTATTGACTCTGAGACCAAGAAGGA  
GCTCCTGGGGACCTACATTAAACAGGGGACTGAGATCGTCCCTGTTGGTGAGGCGCTGCT  
AGAAAAACCAAAGATGGAGTTGCACATCCCCAAAAACGCAGGACTTCCATGTCTGAGGG  
GATCAAGCAGCTCTTGAAAGATATGTTAGCTGCTAACCACAGGACCGGCTGATGCCTT  
TGAAGTTGAAACCAGAAATGGACAGGTACATGTGCTGCTTAAATTCAGGGCTAAGCAT  
TTTGGGTGATTTTAACTAGGTGATTCTCGGGACCCACAGTCTCACCACGTCTCCTCC  
AGAGGACGGCAGAGGGTACAGGTGGTGGCCTGGCCGTTGGCGATCTCCCGACAGCTGGA  
TCCGGCAATGTGAAGCTTTTGTGTTGGGTTTCCCGCTTCTTTTGTAGTTTGTCTTTATTTN  
TNCCCTTTTCTTTTCTTTTNTTTNCCACNTNCCTTTTAAATTTAAACCATTGAG  
ACTTCAGAAGAGCAGGACACAATGCTGTGGACAGGCACCAATTTCTTTAAAGAAATCAA  
TGTGGGCAAGGCATATGTGTAAATTTCACTTTTACTTTTATAAGGGGTAGGGAGCTAT  
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TTATGACACCTCACTTCCCTAGAGAAGGCCTGCCTCCCCATAGGGAATCTGGGGGTANCT  
TCTGGAACGGGGCGTGAGGANACAAGGAGCCTCTGGGCCACNCCTCCCTACCAGATGCAG  
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GAGGTGAAGAACCGCC

SEQ ID NO: 98\_AA498104\_M H29974\_M  
CCGTTGCTGCTCCCCCGCCCCCGCAGCCATGGAAACGGGGAAAGAGAACGGAGCCCCG  
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AAGCTGAGGCCGGCGGCCAGGCCATGGATCCGGCTGGGGCCGAGGTCCCGGGCGAGGCC  
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CGCAGTGGGGCCAGGGTGGCAGTCAAGAAGATCCGCTGCGACGCTCCCGAGAACGTGGAG  
TTGGCACTAGCAGAATTCTGGGCCCTCACCAGTCTCAAGCGGCGGCACCAGAATATCGTG  
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GGCTATGCTGAGGAGCCCTGCTATCTCTGGTTTGTCTGAGTACTGTGAAGGTGGAGAC  
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CCAGACAACATCCTGATCACAGAGCGGTCTGGCACCCCCATCCTCAAGGTGGCAGACTTT  
GGACTGAGCAAGGTCTGTGACGGGCTGGCACCCCGAGGCAAAGAGGGCAATCAAGATAAC  
AAAAATGTGAATGTGAATAAATACTGGCTGTCTCAGCTTGTGGCTCAGACTTCTACATG  
GCTCCCGAAGTCTGGGAGGGACACTATACAGCCAAGGCGGACATCTTTGCTCTGGGCATT  
ATCATCTGGGCAATGATAGAAAGAATTACCTTTATTGACTCTGAAACCAAGAAGGAGCTC  
CTGGGGACCTACATTAAGCAAGGGACTGAGATCGTCCCTGTTGGTGAGGCGCTGCTAGAA  
AACCCAAAGATGGAGTTGCATATCCCCCAGAAACGTAGGACTTCCATGTCTGAGGGGGTC

## FIGURE 2XXX

AAGCAGCTCTTGAAAGACATGTTAGCTGCTAACCACAGGACCGACCTGATGCTTTTGAA  
CTTGAAACCCGAATGGACCAGGTACATGTGCTGCTTAAACTCCAGGGCTGAACGTCTTG  
GGTGTTTTTTAACTAGGTTCGATCCTTCGGGACCCACAGTCTCATCGTGTCTCGGACAGGA  
TGGCAGAGGGTACAGGTGGTGGTGTATCTCCTGACAGCTGGACCTCCCAATGTGAAGCT  
CACGCTTGGGCTGCCCCTCTACCCCTCTCTTTCTCCTTCAGTAGAATAATAATTGTTTT  
TCTAAACATTAAACCATCAAGACTTCTGAAGAGCAGAAGGCTACACTCTG

SEQ ID NO: 99\_AA215311\_H

CGRCCGCGCTACGGAAAGCCGGAGGGGGGCGGGGCCGTGCGCGTAAGGGGGTGTGTCCGC  
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TGCCCGATAATGGCGGCCTGCAGAGCCCATGAGAGGGAGAAGCGGCAGCGTCTACCCTGA  
GAAACCTCGACCTTGAAGATGGTGTAGTAGCCAGCCAAAGTACGATCTAATACGGGAGGTA  
GGCCGAGGTAGTTACGGTGTGTGTATGAAGCAGTCATCAGAAAGACCTCTGCACGGGTG  
GCAGTGAAGAAAATTCGATGTACGCACCTGAAAATGTTGAACTAGCCCTTCGTGAGTTC  
TGGGCACTAAGCAGTATCAAGAGCCAAATCCAAATGTGATTCACTTGGAGGAATGCATC  
CTACAAAAGGATGGGATGGTGTCAAAGATGTCCCACGGCTCTAATTCTTCCCTTTATTTA  
CAGCTTGTAGAACTTCATTAAAAGGAGAAATTGCCTTTGATCCCAGAAGCGCCTATTAT  
TTGTGGTTTGTGATGGATTTTTTGTGACGGAGGAGATATGAATGAGTATCTGTTGTCCAGG  
AAGCCCAATCGTAAACTAACACCAGCTTCATGCTTCAGCTGAGCAGTGCCCTGGCTTTC  
TTGCATAAAAACCAGATCATCCACCGAGATCTTAAGCCTGATAACATCCTGATTTCTCAA  
ACCAGGTGGATACCAGTGAAGTGTGAACCTACCCTCAAAGTGGCTGATTTTGGTCTAAGT  
AAAGTTTGTTCAGCCTCTGGGCAGAACCAGAAACCTGTGAGTGTAAACAAGTGTTC  
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ACAGCAAAAAGCTGACATCTTTGCTCTGGGGATTATCATCTGGGCAATGCTGGAAAGGATC  
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GAGATTGTGCCTGTTGGGGAGGCACCTCTGGAAAATCCCAAAATGGAACCTCTCATTCTCCT  
GTGAAGAAAAAATCTATGAATGGGCGAATGAAACAACCTGATTAAGGAAATGCTGGCTGCA  
AACCCTCAGGATCGTCCAGATGCTTTTGAAGTAGAACTCAGATTAGTACAAATTGCATTT  
AAAGATAGCAGCTGGGAAACGTGACACATATTATTTGCAAATACCATGGATGATATGCTG  
CTTCTGTTTAAACAGTGATGCAACATTATGTGGCTGAAAAAGAATATAAAAAGCTAGACTC  
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AAGTTGGCCGTTTTATTAGTATGTTTCAAATGTGTATTACCAATGTGGGTGTAAATTTTT  
AAAAAATGATTATTGATAGAAGTTTGGCAGGAAAATTCTTTAAGAGCTAACAAGAGAAGA  
GAGTCCAGTTTTCTGGAAATATGTCTTTAAGTATTTTAGACATTCTCGTCAGTATTAGG  
AATTTCCATGGGAAAAGAGGTTTGCATGCTGGTAATGCAACCTTTGAACTTTGTAAAGG  
AAACATATATGTATATATTTATGTATATGTAAGTATGTGAATGTGCGCATTTTGCATTCC  
ATATGAAAAAATGCCACGTCTGTTTAAATTATTTGATGTAGGTTTGGGTTTTTGAGATT  
TGCTGGTGAAGTCAGTGACGAAAAATAAACCTTCCCTTATCTTCTACTCTGCCCCCTCCC  
CCTAATGAAATCATATTAAGTNGTTTTTCTNNTTTTTTTGTAAATATACAGCTTTTTTTTT  
TAAGGCATCATTTTCGAGGGTCTAAAATTATCTGGTAAAACAAATGAAATTAAGTGATCC  
AAAGCTGCTGAAGTATGTTTGAAGTCTCCAGTGCCCTATAGCTGCAAGAGTTGAATTAGT  
CATGCAGTCATATGGCAGCAGGTTGGTGATT

SEQ ID NO: 100\_AA018361\_H

GCGGGGCCCTCCGTATCCCCACGTGGGCCCTGCAGGAACTGGCGGGGCGCGTGACCCGGCG  
AGGCCCAGAGACAGGGGAGGGGCGCCGGGAGCCGGGCGGATCCGCGTCCCCGATGCGCGC  
TGCAATTTCCGGCGGGGCGGCGCTGGGGGACGCTGGAGCCACCCAGTGCTCGGCCCGCCCC  
GCAACCCGCCGGAACCGCCGCCCGCAGCGAGGAAGCGCCCGCGCGGGGCGCAGGCGGCCGG  
AATGGCGGGGCCCCGGCTGGGGTCCCCCGCGCCTGGACGGCTTCATCCTACCGAGCGCCT  
GGGCAGCGGCACGTACGCCACGGTGTACAAGGCCTACGCCAAGAAGGACACTCGTGAAGT

## FIGURE 2YYY

GGTAGCCATAAAGTGTGTAGCCAAGAAAAGTCTGAACAAGGCATCGGTGGAGAACCTCCT  
CACGGAGATTGAGATCCTCAAGGGCATTTCGACATCCCCACATTGTGCAGCTGAAAGACTT  
TCAGTGGGACAGTGACAATATCTACCTCATCATGGAGTTTTGCGCAGGGGGCGACCTGTC  
TCGCTTCATCCATAACCCGCAGGATTCTGCCTGAGAAGGTGGCGCGTGTCTTCATGCAGCA  
ATTAGCTAGCGCCCTGCAATTCCTGCATGAACGGAATATCTCTCACCTGGATCTGAAGCC  
ACAGAACATTCTACTGAGCTCCTTGGAGAAGCCCCACCTAAAACTGGCAGACTTTGGTTT  
CGCACAAACATGTCCCCGTGGGATGAGAAGCACGTGCTCCGTGGCTCCCCCTCTACAT  
GGCCCCCGAGATGGTGTGCCAGCGGCAGTATGACGCGCGGTGGACCTCTGGTCCATGGG  
GGTCATCCTGTATGAAGCCCTCTTCGGGCAGCCCCCTTTGCCTCCAGGTCGTTCTCGGA  
GCTGGAAGAGAAGATCCGTAGCAACCGGGTCATCGAGCTCCCCCTTGCGGCCCTGCTCTC  
CCGAGACTGCCGGGACCTACTGCAGCGGCTCCTGGAGCGGGACCCAGCCGTGCGATCTC  
CTTCCAGGACTTCTTTGCGCACCCCTGGGTGGACCTGGAGCACATGCCAGTGGGGAGAG  
TCTGGGGCGAGCAACCGCCCTGGTGGTGCAGGCTGTGAAGAAAGACCAGGAGGGGGATT  
AGCAGCCGCCTTATCACTCTACTGCAAGGCTCTGGACTTCTTTGTACCTGCCCTGCACTA  
TGAAGTGGATGCCAGCGGAAGGAGGCAATTAAGGCAAAGGTGGGGCAGTACGTGTCCCG  
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CTCTGCCCCGAGACCTGCTCAGAGAGATGGCCCCGGGACAAGCCACGCCTCCTAGCTGCCCT  
GGAAGTGGCTTCAGCTGCCATGGCCAAGGAGGAGGCCGCCGGCGGGAGCAGGATGCCCT  
GGACCTGTACCAGCACAGCCTGGGGGAGCTACTGCTGTTGCTGCGGAGCCCCCGGGCCGG  
AGGCGGGAGCTGCTTCACTGAGGTTGAGAACCTCATGGCCCCGAGCTGAATACTTGAAG  
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TCTGTTGCTAGCTCTTGACCCCTTCACTGACCCCTAGAAGAATGATTGGACAGATGTGAGC  
CATCTGGAGCAGAGGGGCACTAACCAGGCTGACGCCAAGAATGAAGTGGCCCACTGCAG  
CCCTGGCGAGCAGGCTTCTTGGATGGACAGTGTGAGACCCCCATATCCCAGAGTCCCCA  
GCCTCCCTCAGGTTACTCTGCACCCACAGATGGTTTGATGGCTGTGCTGTATACTGGAG  
GGGAGGGCAGGACTCTGGGAGAACAGCACTTCTTTCATGAGACCTTTGTTACTCGGTGGT  
TACTGGGTCTGTGCCTGTCCGTTTTGGGGCATGCAGCCCTCTATCATTTTTTGCTCCGA  
GAAGAGGGCAAGGGGCCCCCGCAGGGTACTTCTGTGCTTGCCCTCGCCCTGCCAGCAGGC  
AGCTGTGCCCTGGCCTGCCCTTCCCGGGACCCCTTATTCCAACCTCAGCTCCTCTTTGCA  
CTGGAATGGGGCACTCCAACACCCCTCAGGGACACCCTCCCCACAGTATGCACTCAGCC  
CCACAGAACCCACCACTCTTCTGGGAACCTCACACCTGCCCGCCATCTTGGTACTTTAGG  
TTAATCCCTCAAGCATGAAAGCTGGATCTTTTGGGGTTTAAGAAGCCCAAGCCTTGTTCC  
TGCCCTGGCCTAGGGAGCACTCAGGAGGGTTCTTGGTCTCATCTCTCCCACCTCCGTT  
CCCTCTGGGCCCCACACTAGCCACAGCGCGGGCCTTGTGCTGGAGTTTGAGCCTGGGACA  
GGGAGAGGGAGGCTTGGAGACAGTCTGACCCAGTGGCCTCTAGGCCACCCACTTCTAGGC  
CTGCCCTGCCGCCGTGGAGCCCTGGGCAAGCTCTTCCCCTTTCTGGGCCTGGGTCTCCC  
CATCTCTTCAATGGGGCTGATACCTTACAGCCCACAGCATGGGCACCTTATGAGGACAAA  
GTGAATTTAACCCTGGAAAAGAATGTATTTGAGAGTTTCTTTTAAATAATCAGCGGGTGT  
GGTGATTTGTAGCCCTTCTGCCCTTAAATGCTTCTTGGGCAAGAGCTGTCTGTCTCCC  
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SEQ ID NO: 101\_AA311714\_H

TGGACCTGTCTGAGGCAGAGGCCGAGATGCGCGCAACCGCGGGAGCAGCCAAGTGGACT  
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GAAGTCGGCCCAGAGATGGAAAACCTTATTCTGTATGAGGAGATCGGAAGAGGAAGCAAG  
ACTGTTGTCTATAAAGGGCGACGGAAGGGAACAATCAATTTGTAGCCATTCTTTGTACT  
GATAAGTGCAGAAGGCCTGAAATAACCAACTGGGTCCGTCTCACCCGTGAAATAAAACAC  
AAGAATATTGTAACCTTTTCATGAATGGTATGAAACAAGCAACCACCTCTGGCTAGTGXAT  
GAAAACCTCCCAGAAGATGTTGTGAGAGAATTTGGAATTGACCTGATTAGTGGATTACAT  
CATCTTCATAAACTTGGCATTCTCTTTTGTGACATTTCTCCTAGGAAGATACTCTTGGA



## FIGURE 2ZZZ

GGGCCTGGCACACTGAAGTTTAGCAACTTTTGCTTGGCAAAAGTGGAAGGTGAAAATTTG  
GAAGAGTTCTTTGCTTTGGTGGCAGCAGAGGAAGGAGGAGGTGATAATGGGGAAAATGTC  
CTGAAGAAAAGCATGAAAAGTAGAGTCAAAGGATCTCCTGTATATACAGCACCAGAAGTT  
GTGAGGGGTGCTGACTTTTCCATCTCCAGTGACCTCTGGTCTTTGGGCTGTCTGCTTTAT  
GAAATGTTTTTCAGGAAAACCTCCATTCTTCTCAGAAAGTGTTTCAGAAATTAAGTAAAAG  
ATCTTATGTGAAGATCCTTTGCCACCTATTCCGAAAGATTCTTCTCGTCCTAAAGCTTCT  
TCAGATTTTATTAATTTGCTTGATGGGTACTTCAAAGAGATCCTCAGAAAAGATTGACT  
TGGACAAGGCTACTGCAGCATTCAATTTTGAAGAAAAGCTTTTGCTGGAGCAGATCAGGAA  
TCAAGCGTGAAGATCTCAGTCTCAGCAGAAACACTATGGAGTGTTCTGGGCCACAAGAT  
TCCAAGGAGCTTTTGCAGAACTCTCAGAGTAGACAAGCAAAAGGGCACAAGAGTGGTCAA  
CCACTAGGTCACCTTTTTCAGACTAGAAAATCCAAGTGAAGTTTCGGCCTAAGAGTACTCTT  
GAGGGTCAATTGAATGAATCCATGTTTCTTCTCAGTTCTCGTCCTACTCCCAGAACTAGC  
ACTGCAGTGAAGTAAGTCCCTGGTGAGGATATGACTCACTGTTCAACACAGAAGACTTCT  
CCTCTGACCAAGATTACAAGTGGACACCTGAGTCAGCAGGACCTGGAATCCCAGATGAGA  
GAGCTTATCTACACGGACTCAGATCTTGTTGTCACCCCCATTATCGACAATCCAAAGATA  
ATGAAACAGCCACCAGTTAAATTTGATGCAAAAATATTGCATCTACCAACATATTTCAGTG  
GATAAGTTATTATTTCTGAAAGATCAAGATTGGAATGACTTTTTTGCAACAAGTGTGCTCG  
CAGATCGACTCCACTGAGAAGAGCATGGGGGCCTCCCGAGCCAAGCTGAATCTCCTTTGC  
TATTTGTGCGTGGTGGCTGGTCACCAGGAGGTGGCCACCAGGCTCCTCCATTCCCCCCTG  
TTCCAATTGCTAATCCAGCATTGCGGATAGCTCCAACTGGGATATACGGGCCAAGGTT  
GCTCACGTGATTGGTTTACTGGCTTCGCACACAAGTGAAGTCCAGGAAAATACACCTGTT  
GTTGAGACTACAAGCTCCATTGGAATCGGGATTTTGAAGTGTCTTGTTCAACACTCCACT  
CCAGTGCCTAGACAGTGCCTTGTGTATGTATAGATACTGACAAATATTTCAAATAAATA  
AAACTGTATCAGCATT

SEQ ID NO: 102\_SGK384\_H

TCTTTGGCCACGTGCTGAGGGCGCGGCAGATCCTGACGGAGCCAGAAGTGC GCGACTAC  
CTGCGGGGCCTGGTCAGCGGCCTGCGCTACCTGCACCAGCGGTGCATCCTGCACCGC

SEQ ID NO: 103\_AA210451\_M SGK384\_M

GGTCTGCTGCATGGATAATGGACTGGAACACAGAAAGACCATGCAGGGTTTCGGCTGTAGA  
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AACCTGCTGGGAGAAAAAGAACTGCTGAAGGGACTGACATGGGACAGCAACATGGAA  
CCAGGAATGGTCTCACGCATAGAGAGCTCCCCGGGGCGTGGGGCTGCTGCTCGCCATGG  
CCCTTATGAACGTGGCGCTCTACCTCTGCCTTGATCAGCTTTTCATCTCCCCTGGACGAT  
CCACCGCGGACTCTAGGCGCTGTCTCCGGGCTACTTCAGAATGGGGCGGATGAGAACT  
GCTCACGCTGGCTGTCTGTGAAGAGCTGAGGACAGAAGTCAGGCAGCTGAAGCGCGTTG  
GGGAGGGAGCCGTGAAGAGAGTCTTTCTGTCTGAATGGAAGGAACACAAAGTCGCTCTCT  
CCCCGCTCACACAGGCTGGAGATGAAGGAGGACTTCCTGCATGGGCTGCAGATGCTGAAGT  
CTCTACAGAGTGAGCACGTGGTCACGCTGGTGGGCTACTGTGAGGAAGATGGCACTATTC  
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TCATTAATCTATCTGCATCACAGCCCCCTGGGCACGAGGGTCATGTGTGACTCTAACGACC  
TGCCCAAAACATTGTCCCAGTACCTGCTAACAAGTAACCTTCAGCATTGTGGCAAACGACC  
TGGACGCTCTGCCCCCTGGTAGACCATGACTCTGGGGTACTTATAAAGTGTGGCCACAGAG  
AGCTCCATGGGGATTTTGTGGCTCCAGAGCAGCTGTGGCCCTACGGAGAAGACACGCCCT  
TCCAAGACGATCTCATGCCTTCCTACAATGAGAAGGTTGACATCTGGAAGATTCCAGATG  
TCTCCAGTTTCTCTTGGGGCACGTGGAAGGGAGTGATATGGTTAGATTCCATTTGTTTG  
ATATCCATAAGGCGTGCAAGAGCCAGATCCCGGCAGAAAGACCCACTGCTCAGAACGTGC



## FIGURE 2AAAA

TAGACGCTTACCAGAGGGTTTTCCATTCACTCCGAGACACTGTGATGTCGCAGACGAAAG  
AAATGCTGTAAAAATGAGCCATCGAGTGACGTGCTTGATGGCTGAATGGCATCCCAGCTG  
TTCCGCTCTTGATGATGGAAGAGCTTTGCATGGATGGATGTTGACCCTGGCTGTTACGCC  
ACGTAGGCCTCCTCTACGTCTGCCTGCATGTTTGAGTGTTCTGCTCTCCTGGCAGCCCGG  
ATGGAAGCTGCCAAGCGAGAAAGCCTGGCTTCAGGATGCTCCCTGGTGAAGATGCAGAGG  
ATTCTGGATCTGCATAGTTTCAAGGGAGTGATCAAACGGTGACCTTGAAGACATGCTGCC  
TGCCTTGGTAACTTTTTATAGACTAGTAGGAAACAGAAATCTTTTGGGGGAGGGGGGGAC  
AACCCTAGTTCCTCAGAGACAATTTCTTCTCATTGAGAAAGCCCTGTTGGAAGCTGGG  
GATGTTTTAACTCCGTGGCAGGGCACTTGCCTAGTTGTGTGCAAAGCCTTGGATCTGACC  
CATGGCATGTGCACACACAAATGCTCAAAGAAAATCCCAGACGCCAGAAAGTGTGCCCC  
TTTCTTGTCATAAGGTCAATTGTGTCAGTACCGGAGATGATTTTTTTTATGAAGCGTTTATG  
CTGACTCGTGTCACTGAGCCAAGTGTGCATGGTTCGTTAGCTACTTTGTGGGTCTTCTCTT  
CTTTCTACCCTACTTCTTCCCTTTCCACCCCCTAACACTAGATAGGAGAGAGGAGAGAGA  
AAGGAAAGTGGGCACCTGTTATATTGTTGGACGACTTCTTGCTGATTAAAGGGGTGTGAGT  
TCCTTGGAGCAATGATCTTTGCTGCCAAGATATCTCATTTCTTCTTGTTTCTTCTTCGCC  
CACGACCACTTCACAAACACCGACCAACAGCAAACAACAACCCACCCCGCTTCTCGGGGG  
CCCTAGCACTTATGTACTTCTGAAAAGTCCCCAGAAATTCCAATCATCACACACTCAGAG  
AAACTGTCTGCTGCTGGCAAACTACACCCCTGCTAGAGCATGAGGCAAATCATAGTCAG  
CTGCTGTGGACAGTCTGAAGCAGCCTGGCATCCCACACCTGAGATTAACAAACAAACATT  
CTTACCTGTGTTTTGTTTTTGTTTTAAAGAAACCAAAGTGCACCAAGATAGCATGCTCTTG  
AGATTGTGGCTGTCTAGAGATTTTTTGAACAGCAAGTTGAAGGAACTTTCTTACCTGCCT  
TGAATGGTGCTTTGAACTTCCTGCTGACCTGGAGTTTCTGTGTGAATATTTCTATCCAGT  
GTCCCCCTGTACCGGAAAGTACAAAGTCTGCTCTGGGCTTGCATGCCTGAACACTTTAAA  
ACACTGTGGAGCCAGGAATAATGGTACCCACCTGTAATCCCAGCACCTGGGAGACAGGAG  
GAACCAGGAGTTCAGGGTTATCCTGGGCTATATACCGTGACCCTGTCTACCCCCACACCC  
CAATAAAAAAACAAAAAGGTC

SEQ ID NO: 104 SGK071\_2\_H

GAGGTGGTGGCTGTGCAGATGATGGTGGAAATGCATGGATGACCATTACGCCAGTCAGGCC  
CTGGAGGAGCTGATGCCACTGCTGAAGCTGCGGCACGCCCACATCTCTGTGTACCAGGAG  
CTGTTTCATCACGTGGAATGGGGAGATCTCTTCTCTGTACCTCTGCCTGGTGTGAGGTTT  
AATGAGCTCAGCTTCCAGGAGGTCATTGAGGATAAGAGGAAGGCAAAGAAAATCATTGAC  
TCTGAGTGGATGCAGAATGTGCTGGGCCAGGTGCTGGACGCGCTGGAATACCTGCACCAT  
TTGGACATCATCCACAGGAATCTCAAACCTCCAACATCATCCTCATCAGCAGTGACCAC  
TGCAAATGCAGGACCTGAGTTCCAATGTGCTAATGACAGACAAAGCCAAATGGAATATT  
CGTGCGGAGGAAGACCCCTTTTCGTAAGTCTGGATGGCCCCCTGAAGCCCTCAACTTCTCC  
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TCCTTCATGGATGGCACAGAAGCCATGCATCTGCGGAAGTCCCTCCGCCAGAGCCCAGGC  
AGCCTGAAGGCCGCTCCTGAAGACAATGGAGGAGAAGCAGATCCCGGATGTGGAAACCTTC  
AGGAATCTTCTGCCCTTGATGCTCCAGATCGACCCCTCGGATCGAATAACGATAAAGGAC  
GTGGTGACATCACCTTCTTGAGAGGCTCCTTCAAGTCTCTGTCGTCTCTGACCCTG  
CACCGGCAGATGGTGCCTGCGTCCATCACCGACATGCTGTTAGAAGGCAACGTGGCCAGC  
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TTGGCATCCTATTGTTTAGTTCCAGAGGGTTCATTATTTATGCCCCTGGCCTTGCTCCAC  
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CTGTGTGCTGCTCCCTGCTGCTGCACCTCCTGGGCCAAGCGCTGGTGCACCACCCGGAA  
GCCAAGGCTCCCTGCAACCAAGCCATCACCTCCACCTGCTGAGTGCTCTTCAGAGCCAC  
CCCGAGGAGGAGCCACTTCTTGTCATGGTCTACAGCCTGCTAGCCATCACCACAACCCAG

## FIGURE 2BBBB

GAGTCAGAGTCACTGTCAGAGGAGCTGCAGAACGCTGGGCTGCTGGAGCACATCCTGGAG  
CACCTCAACAGCTCCCTCGAAAGCAGGGACGTCTGCGCCAGCGGCCTGGGCTGCTCTGG  
GCCCTCCTGCTGGACGACCCCATCTTGGCACTCCAGCGCCCCAGGAAAAAGAGAGCTCCA  
AACCACGGAAAGCCCCGGGAAACCCAAGAACCCTGCCAGCACCCAAAGTATCATTTGTGAAC  
AAGGCCCCCTTGGAGAAGGTCCCGGACCTCATCAGCCAGGTGTTGGCCACCTACCCTGCG  
GATGGGGAAATGGCAGAAGCCAGCTGCGGAGTCTTCTGGCTGCTGTCCCTGCTGGGCTGC  
ATCAAGGAGCAGCAGTTTGAACAAGTGGTGGCGCTGCTCCTGCAAAGCATCCGGCTGTGC  
CAGGACAGAGCCCTGCTGGTGAACAATGCCTACCGGGGACTGGCCAGCCTGGTGAAGGTG  
TCAGAGCTGGCGGCCCTTCAAGGTGGTGGTGCAGGAGGAGGGCGGCAGTGGCCTCAGCCTC  
ATCAAGGAGACCTACCAGCTCCACAGGGACGACCCGGAGGTGGTGGAGAACGTGGGCATG  
CTGCTGGTCCACCTGGCTTCCTATGAGGAGATCCTGCCGGAGCTGGTGTCCAGTAGTATG  
AAGGCCCTGCTCCAGGAGATCAAGGAGCGCTTCACCTCCAGCCTGGTGAAGTACAGCAGC  
GCCTTCAGCAAACCAGGCCTCCCTCCAGGTGGAAGCCCCCAGCTGGGGTGCACCACGTCT  
GGGGGACTGGAATAG

SEQ ID NO: 105\_AA118352\_M SGK071\_M

CAGAAGAAGACCCCTGCCAGAAGTCCTGGATGGCTCCTGAAGCTCTCAAATTCTCCTTCT  
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TCCTGAACGACACAGAAGCCATGCAACTGCGGAAGGCCATCCGCCATCATCCAGGCAGCC  
TGAAGCCCATCCTGAAAACCATGGAGGAGAAGCAAATCCCTGGTACAGATGTCTACTATT  
TGCTTCTGCCCTTCATGTTGCATATCAACCCCTCCGATCGACTGGCAATCAAGGATGTGA  
TGCAAGTCACCTTCATGAGCAACTCCTTCAAAGCTCCTCTGTTGCGCTGAATATGCAGC  
GGCAGAAGGTCCCCATCTTCATCACTGACGTGCTGCTTGAAGGCAACATGGCCAACATCT  
TAGGCAGCTGGCTGTGTGCTTCCTTTGTGAACGACAGCAGGCACTGTGACTCAGGGATTG  
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TCAGCATCATAAAGCAGCATGGGCGGATCCTGGATATTCTGCTCAGCACCTGCTCCCTTC  
TGCTGCGTGTCTTGGCCAAGCACTGGCAAAGGACCCAGAAGCTGAGATCCCAAGGAGCA  
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GGGACATCTGCCTCTCTATCCTGAGCCTGCTCTGGTCCCTCCTGGTAGATGTTGTCACTG  
TGGACAAAGAGCCCTTGGAGCAGCTCTCTGGCATGGTCACCTGGGTGCTGGCTACTCATC  
CGGAGGACGTGGAATAGCAGAGGCTGGCTGTGCGGTGCTCTGGCTGCTGTCTTGTGG  
GCTGCATAAAGGAGAGTCACTTGTGAGCAGGTGGTAGTGCTGCTCCTGAGAAGCATCCAGC  
TGTGCCCTGGCAGAGTACTGCTGGTGAACAATGCATTCCGTGGCTTGGCCAGCCTCGCAA  
AGGTGTCCGAAGTGGTGGCCTTCCGAATAGTAGTACTGGAAGAGGGCAGCAGCGGCCTCC  
ACCTCATCCAAGATATCTACAAGCTCTACAAGGATGACCCTGAGGTGGTGGAGAACCCTCT  
GCATGCTGTTGGCCCATCTGACCTCCTACAAGGAGATCCTGCCAGAGATGGAGTCTGGAG  
GCATCAAAGACCTAGTCCAGGTGATCCGGGGGCGCTTTACCTCCAGCCTGGAGCTGATTT  
CTTACGCTGATGAGATACTCCAGGTACTGGAAGCAAATGCACAACCTGGCCTCCAGGAGG  
ATCAGCTTGAGCCTCCTGCAGGGCAGGAAGCCCCACTGCAGGGAGAGCCCTCTTCAGGC  
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SEQ ID NO: 106\_018653.9\_H

GGCCGGGGTCCGGGCGCGGGGCATGCGCGCGGGCTGGGCAGGGGGCCGGCGGGGCGCAGA  
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## FIGURE 2CCCC

CGCCTCCTTCCTGCTGGGCTCCGTCCTCAACGTGCTCTTCGCTCCGGGTCCGAGCCTCCG  
AGGCCAGGCCAGTCCCCTGAGCCTTCGCCGGCCCCGGGTGCGGGCCGTGCGGGGGCCGC  
GGGAGCTGGCCCCGGCAGATCCGGGCGCGCTACGAGGAGGTGCAGCGCTATTCCCGCGGG  
GGCCCCGGGCCCCGGGGCGGGCCGGCCGGAGCGGCGGCCTGATGGACCTGGCTCCGGGC  
GGCCCCGGCCTGCCGCGCCCCCGGCCCCCTTGGGCCCCGGCCCCGTGTCCGACGGCGCCCCA  
GGCTGGCCCCCGGCTCCCCGGCCCAGGCTCCCCCGGCCCCGGCCCCGCGCCTGGGCTGCGCC  
GCGCTTCGCAACGTGTCCGGCGCGCAGTACATGGGCTCAGGCTACACCAAGGCCGTGTAC  
CGGGTCCGCTGCCCGGCGGTGCCGCGGTGGCGCTCAAGGCGGTGGACTTTAGCGGCCAC  
GATCTGGGCAGCTGCGTGCGCGAGTTCGGGGTACGGAGGGGCTGCTATCGGCTGGCGGCC  
CACAAGCTGCTTAAGGAGATGGTGTGCTGAGAGCGGCTGCGGCACCCCCAACGTGCTGCAG  
CTCTATGGCTACTGCTACCAGGACAGCGAGGACATCCAGACACCCTGACCACCATCACG  
GAGCTGGGCGCCCCGTAGAAATGATCCAGCTGCTGCAAACTTCCTGGGAGGATCGATTTC  
CGAATCTGCCTGAGCCTGGGCGCCTCCTCCACCACCTGGCCCCACTCCCCACTGGGCTCC  
GTCACTCTGCTGGACTTCCGCCCTCGGCAGTTTGTGCTGGTGGATGGGGAGCTCAAAGTG  
ACGGACCTGGATGACGCACGTGTGGAGGAGACGCCGTGTGCAGGCAGCACCGACTGCATA  
CTCGAGTTTCCGGCCAGGAACCTTACCCTGCCCTGCTCAGCCAGGGCTGGTGCGAGGGC  
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CACAGTGCCCCGCTTCACTGCGTCCTCTGCTGGACAGCATCGTCAACGCCACAGGAGAG  
CTCGCCTGGGGGGTGGACGAGACCCTGGCCAGCTGGAGAAGGTGCTGCACCTGTACCGG  
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GACAGCACCATCCCCAGGAAGACTACCGCTGCTGGCCATCCTACCACCACGGGAGCTGC  
CTCCTTTCAGTGTTCAACCTGGCTGAGGCTGTGGATGTCTGTGAGAGCCATGCCAGTGT  
CGGGCCTTTGTGGTCACCAACCAGACCACCTGGACAGGTCCGCAGCTGGTCTTTTTCAAG  
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AGATGCTCCAGGATGTGGGTGATTCTGTACCTGGGGAGGCTATCTCTGACCTCCCGACAG  
GGGACACTCCAGGCCAGCCAGGGGTCAGGGGCAGAGGTGCACACCTCAGCATGAGCCA  
AGACTGGGGTCAGGGAGCAGGTGTGGTTTGAGCCAGGACCTGGGGCGGGGGTGGGGCCGG  
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CCCTTCCTCGAGTTTGAATATCCAGAATCTTTTGTACTTCTTGTGGTTAAATTGTTTAT  
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SEQ ID NO: 107\_AA396601\_M

CCACGCGTCCGGGCTGCGCCGCGCTCCGCAACGTGTCTGGCGCGCAGTACGTGGGCTCAG  
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GGCACCCCAACGTGCTGCAGCTCTATGGCTATTGCTACCAGGACAGTGAGGGCATCCAG  
ACACGCTGACCACCATCACAGAGCTGGGTGCCCCCTGTGGAGATGATCCAGCTGTTGCAGA  
CTTCCTGGGAGGATCGATTCCGAATCTGCCTCAGCCTTGGCCGCTCCTCCACCACCTGG  
CCCACTCCCCGCTGGGCTCGGTCAACCCTGCTTGACTTCCGCCCTCGGCAGTTTGTGCTAG  
TGAACGGGGAGCTGAAAGTGACAGACCTGGATGATGCCCCGCGTGGAAGAGACACCGTGCA

## FIGURE 2DDDD

CCAGCAGTGCCGACTGCACGCTAGAGTTTCCAGCCAGGAACCTTCAGCCTGCCCTGCTCGG  
CCCAGGGCTGGTGCAGGGGCATGAATGAGAAACGGAACCTCTACAATGCCTACAGGTTCT  
TCTTCACATACCTCCTGCCACACAGTGCCCCGCCTTCCCTCCGACCTCTCCTGGATAGCA  
TCGTCAATGCCACGGGAGAGCTCGCCTGGGGGGTGGATGAGACCCTGGCCCAGCTGGAGA  
CAGCGCTACACTTGTTCGAAGTGGGCAGTACCTGCAGAACTCTACAAGCAGCAGGGCTG  
AGTACCAGCGCATCCCGGACAGTGCCATCACACAGGAGGACTATCGCTGCTGGCCATCCT  
ATCACCACGGCGGCTGCCTCCTGTCCGTGTTCAACCTGGCTGAGGCTATAGATGTCTGTG  
AGAGCCATGCTCAGTGTCTGTCCTTTGTGGTCACCAACCAGACCACCTGGACAGGTCGGA  
AGCTGGTCTTTTTTAAGACTGGATGGAACCAAGTGGTCCCTGATGCCGGCAAGACCACAT  
ATGTGAAGGCCCTGGTTGACTGGTTGTGGGCTCAGCTGACCAGCTGGGCTTGCCTGCTG  
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CTCAGGCTGGTCTTAACTGGGACAGTCCCGTGGGCAGCCCATTACTGCATTTCATGCTTTG  
AGAATGTAGCCAGAACACTGCTGCTGCATAAGCCACCGTGGGCAGGAGCTGCCTGGGGAC  
AACCAGTCTCAGAGTGCTCTCTCAGCTCAGCTCCGCTCCAAATGGAGAGCGCGGGATGCG  
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TGGAGGAGCAGATTGCATTTGAGCCAGGACTGGGGTGGGGTAGGGTCGGGGCCTCTCTG  
CCTCATTTGCTTTCAGTGAAAGCCAGGGAGCAGCCGAGCCAGGCTCCTCCCCTCCTGG  
AGGCCAGGCTCCTCCCCCTCCTGGAGGCCAGGCTCCTCCCCCTCCTGGAGTTTTCGTACC  
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SEQ ID NO: 108\_VRK3\_H

ATGATCTCCTTCTGTCCAGACTGTGGCAAAAGTATCCAAGCGGCATTCAAATTCTGCCCC  
TACTGTGGAAATTCTTTGCCTGTAGAGGAGCATGTAGGGTCCCAGACCTTTGTCAATCCA  
CATGTGTCATCCTTCCAAGGCTCAAAGAGAGGGCTGAACTCCAGTTTTGAAACCTCTCCT  
AAGAAAGTGAAATGGTCCAGCACCGTCACCTCTCCCCGATTATCCCTCTTCTCAGATGGT  
GACAGTTCTGAGTCTGAAGATACTCTGAGTTCTCTGAGAGATCCAAAGGCTCCGGGAGC  
AGACCCCCAACCCCCAAAAGCAGCCCTCAGAAGACCAGGAAGAGCCCTCAGGTGACCAGG  
GGTAGCCCTCAGAAGACCAGCTGTAGCCCTCAGAAGACCAGGCAGAGCCCTCAGACGCTG  
AAGCGGAGCCGAGTGACCACCTCACTTGAAGCTTTGCCCACAGGGACAGTGCTGACAGAC  
AAGAGTGGGCGACAGTGGAAGCTGAAGTCCTTCCAGACCAGGGACAACCAGGGCATTCTC  
TATGAAGCTGCACCCACCTCCACCTCACCTGTGACTCAGGACCACAGAAGCAAAAGTTC  
TCACTCAAACCTGGATGCCAAGGATGGGCGCTTGTTCAATGAGCAGAACTTCTTCCAGCGG  
GCCGCCAAGCCTCTGCAAGTCAACAAGTGAAGAAGCTGTACTCGACCCCACTGCTGGCC  
ATCCCTACCTGCATGGGTTTCGGTGTTCACCAGGACAAATACAGGTTCTTGGTGTACCC  
AGCCTGGGGAGGAGCCTTCAGTCGGCCCTGGATGTCAGCCCAAAGCATGTGCTGTGAGAG  
AGGTCTGTGCTGCAGGTGGCCTGCCGGCTGCTGGATGCCCTGGAGTTCCTCCATGAGAAT  
GAGTATGTTTCATGGAAATGTGACAGCTGAAAATATCTTTGTGGATCCAGAGGACCAGAGT  
CAGGTGACTTTGGCAGGCTATGGCTTCGCCTTCCGCTATTGCCCAAGTGGCAAACACGTG  
GCCTACGTGGAAGGCAGCAGGAGCCCTCACGAGGGGGACCTTGAGTTCATTAGCATGGAC  
CTGCACAAGGGATGCGGGCCCTCCCGCCGAGCGACCTCCAGAGCCTGGGCTACTGCATG  
CTGAAGTGGCTCTACGGGTTTCTGCCATGGACAAATTGCCTTCCCAACACTGAGGACATC  
ATGAAGCAAAAACAGAAGTTTGTGATAAGCCGGGGCCCTTCGTGGGACCCTGCGGTAC  
TGGATCAGGCCCTCAGAGACCCTGCAGAAGTACCTGAAGGTGGTGTGAGCCCTCACGTAT  
GAGGAGAAGCCGCCCTACGCCATGCTGAGGAACAACCTAGAAGCTTTGCTGCAGGATCTG  
CGTGTGTCTCCATATGACCCCATTTGGCCTCCCGATGGTGCCCTAG

## FIGURE 2EEEE

SEQ ID NO: 109\_S71575\_M VRK3\_M

CCATCCCCACCTGTATCGGCTTTGGCATTACCAGGACAAGTACAGGTTCCCTAGTATTCC  
CCAGCCTGGGGAGGAGCCTTCAGTCAGCCCTGGATGACAACCCAAAGCATGTGGTATCAG  
AGAGATGTGTGCTTCAGGTGGCCTGCAGGCTGCTGGATGCTCTGGAGTATCTCCATGAAA  
ATGAGTATGTTACGGGAACCTGACAGCTGAGAATGTCTTTGTGAATCCAGAGGATCTGA  
GCCAGGTGACCCTGGTGGGCTATGGCTTCACCTACCGATACTGCCCAGGTGGCAAACACG  
TGGCCTACAAAGAAGGCAGCAGGAGTCCACACGATGGGGACTTGGAGTTCATTAGCATGG  
ACCTGCACAAGGGATGCGGACCCTCCCGCCGAGCGATCTCCAGACCTTGGGCTACTGTA  
TGCTCAAGTGGCTTTATGGGTCCCTGCCATGGACAAATTGCCTTCCCAACACCGAAAAGA  
TAACTAGGCAGAAGCAGAAGTATCTGGACAGCCCCGAGCGCCTCGTGGGACTGTGTGGCC  
GCTGGAACAAGGCCTCAGAGACCCTGCGGGAGTACCTGAAGGTGGTGATGGCCCTCAATT  
ATGAGGAGAAGCCACCCTATGCCACGCTGAGGAACAGCCTAGAAGCTCTGCTGCAGGATA  
TGCGGGTGTACCCCTATGACCCTCTGGACCTCCAGATGGTGCCTTAGATGGAATCCAGAG  
CTTCCGACTTGCAGCTTGAAGTAGAACATGAAGTAGTGTGACTGGAGGCCTGTTTGAAC  
CATAGCTCCTAAAAGAATCCCTTGAATGTGCATTCTCACCGCTCCCTTAGGACATATGAA  
TCAGCACTTGTGTTGGGGAACCTGAGTCATGTGTAATGTGAACTCCTCCCTGTCTC  
AGCTCTGGCAGCTGTGGATGGAGGTAAGTGGATGCTGGCGGCGGCGGCGGCGAGCAGCCAC  
TCCACTCCCTATGGCATTCTGTGATGGCATAATAAACTGTTTTTAATC

SEQ ID NO: 110\_AA45427\_H

ATGGGCCACGCGCTGTGTGTCTGCTCTCGGGGAAGTGTGTCATTGACAATAAGCGCTAC  
CTCTTCATCCAGAACTGGGGGAGGGTGGGTTCAGCTATGTGGACCTAGTGGAAGGGTTA  
CATGATGGACACTTCTACGCCCTGAAGCGAATCCTGTGTACAGAGCAGCAGGACCGGGAG  
GAGGCCAGCGAGAAGCCGACATGCATCGCCTCTTCAATCACCCCAACATCCTTCGCCTC  
GTGGCTTACTGTCTGAGGGAACGGGGTGCTAAGCATGAGGCCTGGCTGCTGCTACCATTC  
TTCAAGAGAGGTACGCTGTGGAATGAGATAGAAAGGCTGAAGGACAAAGGCAACTTCCTG  
ACCGAGGATCAAATCCTTTGGCTGCTGCTGGGGATCTGCAGAGGCCTTGAGGCCATTCTAT  
GCCAAGGGTTATGCCACAGAGACTTGAAGCCCAACATATATTGCTTGGAGATGAGGGG  
CAGCCAGTTTTAATGGAAGTGGGTTCATGAATCAAGCATGCATCCATGTGGAGGGCTCC  
CGCCAGGCTCTGACCCTGCAGGACTGGGCAGCCAGCGGTGCACCATCTCCTACCGAGCC  
CCAGAGCTCTTCTGTGTCAGAGTCACTGTGTCATCGATGAGCGGACTGATGTCTGGTCC  
CTAGGCTGCGTGCTATATGCCATGATGTTTGGGGAAGGCCCTTATGACATGGTGTTCCAA  
AAGGGTGACAGTGTGGCCCTTGCTGTGAGAACCAACTCAGCATCCCACAAAGCCCCAGG  
CATTCTTCAGCATTGCGGCAGCTCCTGAACTCGATGATGACCGTGGACCCGCATCAGCGT  
CCTCACATTCTCCTCCTCAGTCAGCTGGAGGCGCTGCAGCCCCCAGCTCCTGGCCAA  
CATACTACCCAAATCTGA

SEQ ID NO: 111\_H05721\_H

CCCTGAGGCACCGCCCAAGTTTGGTGTGACCGGCGGGGACGCCGGTGGTGGCGGCAGC  
GACGGCTGCGGGGGCACCGGGCCGCGGCCACCATGGCGGTGCGACAGGCGCTGGGCCG  
CGGCCTGCAGCTGGGTGAGCGCTGCTGCTGCGCTTACGGGCAAGCCCGGCGGGCCTA  
CGGCTTGGGGCGGCGGGCCCGGCGGGGCTGTGTCCGCGGGGAGCGTCCAGGCTGGGC  
CGCAGGACCGGGCGCGGAGCCTCGCAGGGTGGGGCTCGGGCTCCCTAACCGTCTCCGCTT  
CTTCCGCCAGTCGGTGGCCGGGCTGGCGGCGCGGTTGCAGCGGCAGTTCGTGGTGGCGGC  
CTGGGGCTGCGCGGGCCCTTGCGGCGGGCAGTCTTTCTGGCCTTCGGGCTAGGGCTGGG  
CCTCATCGAGGAAAAACAGGCGGAGAGCCGGCGGGCGGTCTCGGCCTGTCAGGAGATCCA  
GGCAATTTTACCCAGAAAAGCAAGCCGGGGCCTGACCCGTTGGACACGAGACGCTTGCA  
GGGCTTTCGGCTGGAGGAGTATCTGATAGGGCAGTCCATTGGTAAGGGCTGCAGTGTGC  
TGTGTATGAAGCCACCATGCCTACATTGCCCCAGAACCTGGAGGTGACAAAGAGCACCGG  
GTTGCTTCCAGGGAGAGGCCAGGTACCAGTGCACCAGGAGAAGGGCAGGAGCGAGCTCC

## FIGURE 2FFFF

GGGGGCCCCCTGCCTTCCCCTTGGCCATCAAGATGATGTGGAACATCTCGGCAGGTTCCCTC  
CAGCGAAGCCATCTTGAACACAATGAGCCAGGAGCTGGTCCCAGCGAGCCGAGTGGCCTT  
GGCTGGGGAGTATGGAGCAGTCACTTACAGAAAATCCAAGAGAGGTCCCAAGCAACTAGC  
CCCTCACCCCAACATCATCCGGGTTCTCCGCGCCTTCACCTCTTCCGTGCCGCTGCTGCC  
AGGGGCCCTGGTCGACTACCCTGATGTGCTGCCCTCACGCCTCCACCCTGAAGGCCTGGG  
CCATGGCCGGACGCTGTTCCCTCGTTATGAAGAACTATCCCTGTACCCTGCGCCAGTACCT  
TTGTGTGAACACACCCAGCCCCCGCCTCGCCGCCATGATGCTGCTGCAGCTGCTGGAAGG  
CGTGGAACCATCTGGTTCAACAGGGCATCGCGCACAGAGACCTGAAATCCGACAACATCCT  
TGTGGAGCTGGACCCAGACGGCTGCCCCCTGGCTGGTGATCGCAGATTTTGGCTGCTGCC  
GGCTGATGAGAGCATCGGCCTGCAGTTGCCCTTCAGCAGCTGGTACGTGGATCGGGGCGG  
AAACGGCTGTCTGATGGCCCCAGAGGTGTCCACGGCCCCGTCTGGCCCCAGGGCAGTGAT  
TGACTACAGCAAGGCTGATGCCCTGGGCAGTGGGAGCCATCGCCTATGAAATCTTCGGGCT  
TGTCATCCCTTCTACGGCCAGGGCAAGGCCACCTTGAAAGCCGCAGCTACCAAGAGGC  
TCAGCTACCTGCACTGCCCGAGTCAGTGCCCTCCAGACGTGAGACAGTTGGTGAGGGCACT  
GCTCCAGCGAGAGGCCAGCAAGAGACCATCTGCCCGAGTAGCCGCAAATGTGCTTCATCT  
AAGCCTCTGGGGTGAACATATTCTAGCCCTGAAGAATCTGAAGTTAGACAAGATGGTTGG  
CTGGCTCCTCCAACAATCGGCCGCCACTTTGTTGGCCAACAGGCTCACAGAGAAGTGTTG  
TGTGGAACAAAAATGAAGATGCTCTTTCTGGCTAACCTGGAGTGTAACGCTCTGCCA  
GGCAGCCCTCCTCCTCTGCTCATGGAGGGCAGCCCTGTGATGTCCCTGCATGGAGCTGGT  
GAATTACTAAAAGAACATGGCATCCTCTGTGTCGTGATGGTCTGTGAATGGTGAGGGTGG  
GAGTCAGGAGACAAGACAGCGCAGAGAGGGCTGGTTAGCCGAAAAGGCCCTCGGGCTTGG  
CAAATGGAAGAACTTGAGTGAGAGTTTCACTCTGCAGTCCTCTGCTCACAGACATCTGAAA  
AGTGAATGGCCAAGCTGGTCTAGTAGATGAGGCTGGACTGAGGAGGGGTAGGCCTGCATC  
CACAGAGAGGATCCAGGCCAAGGCACTGGCTGTCACTGGCAGAGTTTGGCTGTGACCTTT  
GCCCCAACACGAGGAACCTCGTTTGAAGGGGGCAGCGTAGCATGTCTGATTTGCCACCTG  
GATGAAGGCAGACATCAACATGGGTTCAGCACGTTTCACTTACGGGAGTGGGAAATTACATG  
AGGCCTGGGCCTCTGCGTTCCCAAGCTGTGCGTTCTGGACCAGCTACTGAATTATTAATC  
TCACTTAGCGAAAGTGACGGATGAGCAGTAAGTAAGTAAGTGTTGGGGATTTAACTTGAG  
GGTTTCCCTCCTGACTAGCCTCTCTTACAGGAATTGTGAAATATTAATGCAAATTTACA  
ACTGCAGATGACGTATGTGCCTTGAAGTGAATATTTGGCTTTAAGAATGATTCTTCTTAT  
ACTCTGAAGGTGAGAATATTTTGTGGGCAGGTATCAACATTGGGGAAGAGATTTTCATGTC  
TAACTAATAACTTTATACATGATTTTTTAGGAAGCTATTGCCTAAATCAGCGTCAACATG  
CAGTAAAGGTTGTCTTCAACTGACAAAA

SEQ ID NO: 112\_AI086865\_H

AATGAGATGGAGAAGTACGAGCGGATCCGAGTGGTGGGGAGAGGTGCCTTCGGGATTGTG  
CACCTGTGCCTGCGAAAGGCTGACCAGAAGCTGGTGATCATCAAGCAGATTCCAGTGGA  
CAGATGACCAAGGAAGAGCGGCAGGCAGCCAGAATGAGTGCCAGGTCCTCAAGCTGCTC  
AACCACCCCAATGTCATTGAGTACTACGAGAAGTTCCCTGGAAGACAAAGCCCTTATGATC  
GCCATGGAATATGCACCAGGCGGCACTCTGGCTGAGTTTCACTCCAAAAGCGCTGTAATTCC  
CTGCTGGAGGAGGAGACCATCCTGCACTTCTTCGTGCAGATCCTGCTTGCACTGCATCAT  
GTGCACACCCACCTCATCCTGCACCGAGACCTCAAGACCCAGAACATCCTGCTTGACAAA  
CACCGCATGGTCGTCAAGATCGGTGATTTCCGCATCTCCAAGATCCTTAGCAGCAAGAGC  
ACCCCATGCTATATCTCCCCTGAGCTGTGTGAGGGCAAGCCCTACAACCAGAAGAGTGAC  
ATCTGGGCCCTGGGCTGTGTCTCTACGAGCTGGCCAGCCTCAAGAGGGCTTTTCGAGGCT  
GCGAACTTGCCAGCACTGGTGTGAAGATCATGAGTGGCACCTTTGCACCTATCTCTGAC  
CGGTACAGCCCTGAGCTTCGCCAGCTGGTCCTGAGTCTACTCAGCCTGGAGCCTGCCAG  
CGGCCACCACTCAGCCACATCATGGCACAGCCCTCTGCATCCGTGCCCTCCTCAACCTC  
CACACCGACGGCAGAGAAGTCCGTGGCCCCCAGCAACACAGGGAGCAGGACCACAGTGT  
CCGCTGCAGAGAGGCATCATCATGACATTCGGCAGCGGCAGCAATGGGTGCCTAGGCCAT

## FIGURE 2GGGG

GGCAGCCTCACTGACATCAGCCAGCCCACCATTGTGGAGGCTTTGTTGGGCTATGAAATG  
GTGCAGCAAGTGGAGGAGGCCCTGAGCTTCACACTACTAGGCTCTGCACCCCTGGACCAG  
GAGCCTCTGCTGAGTATAGACCTGGGCACTGCTCACTCAGCTGCTGTGACTGGTGAGGAG  
GACTTGGGCTCTGGAGATGTAAACAGGTTACCCAGCTGGGAGAGAGGACATCTGCTGGCT  
GGTGTGGCGTCCAGCACTGATGTGTCTACCTTCTCTGAAGGTGACTGCAAGGAGCCTGAC  
AAGTGCTGCTGGAGACACAAGCAGTGCCTGGGACATCATCTACCTTTTCGCCTCTGAC  
TGTGTCCGCCACAGCCTGCACCTACACTCTGTCAACCACTGCAACTGTAATTCTAGGCTG  
AAGGACTCTTCAGAGGATAGCAGCAGCTCCCGGGGCGCGGGCCCAACCTGCTCCCATGTC  
ATCGAGTCCCTTGCTTTGAGCTCACACCGGAGGAGGAGCATGTGGAGCGATTCCGGTAT  
GGCTGGTGCAAAAGCTACAGACCTGTCTCTGTGGCAGTGATCCACCATCCACTCTACCAT  
GAGTGTGGGGCAGATGATCTAAATGXAAAGAAGAGGAAGAGGAGGAGGAGGAAAAGCAAG  
CCCCCATCCCGACACAGGTGGGGCCCGCCACCGCCTCCCCTGACCTAGGCACCAGCATG  
GCCACTGGTACCCCTGACTCCACAGCGCCCATCACCATCTGGCGCTCTGAGAGCCCCACA  
GGGAAGGGTCAGGGCAGCAAGGTGATCAAGAAGGTAAAGAAGAAAAAGGAAAAAGAGAAA  
GACAAGGAGGAGATGGATGAGAAGGCAAAGCTGAAGAAAAAGCCAAGAAAGGCCAGTTG  
ACTAAGAAGAAAAGCCCGTTAAATTGGAGCCTTCCCGCCAGACGTGAGCCGATCATTA  
AGCGCAAGACAGCTGGCCAGGATGTCCGAGTCCAGCCAGAAAGCCGGGAAGAGCTGGAG  
AGCGAGGACAGTTACAATGGCCGGGGGAGGAGAACTGTCCAGCGAGGATATTGTGGAA  
TCATCATCGCCAGGAAGAGAGAGAAACACAGTCCAGGCCAAAAAGACAGGGGCAAAGCCC  
TCACAAGCCAGGAAGGTAAACAAGAGAAAATCTCCCCAGGATCAAACCCCAACCTCAGT  
TGAGGCCAGGGTGGTCAAGGTGCAGAAATAAATGCCATCGAGCCTGTGGCTGGCCCTCTGC  
TGCTGTTCTCTCCCTCCAACCTGGCTGTTTCTTGCGGGGCAAGGGGTGGGCTCAGGGCTG  
CAGGGGTTTCTCAAAGGCAATCCAGCTTTCACAAAGGAAGCCCATGGGAAGGCAGGTGGG  
AGGGAAAGGAAGGGGCACAGCCCTATTTCTTCTTACCTGCTAGGACAAGGTGGAAGAGTG  
TATCTGGGGTGGGAAGGAGGGCTTCCCTCTCTGCTGCGAGAGACTGGTCTGTGTGAAAT  
CCACTTCTGGGACAGGCAGTACTGTCTGCAGCGATAACCCCAATAAACGGAACTTTTTAA  
CCC

SEQ ID NO: 113\_AA836348\_H

ATGTCCGTGCTGGGCGAGTACGAGCGACACTGCGATTCCATCAACTCGGACTTTGGGAGC  
GAGTCCGGGGGTTGCGGGGACTCGAGTCCGGGGCCTAGCGCCAGTCAGGGGCGCGAGCC  
GGCGGCGGCGCGGCGGAGCAGGAGGAAGTCACTACATCCCCATCCGCGTCTTGGGCGC  
GGCGCCTTCGGGGAAGCCACGCTGTACCGCCGCACCGAGGATGACTCACTGGTTGTGTGG  
AAGGAAGTCGATTTGACCCGGCTGTCTGAGAAGGAACGTCGTGATGCCTTGAATGAGATA  
GTTATTCTGGCACTGCTGCAGCACGACAACATTATTGCCTACTACAATCACTTTCATGGAC  
AATACCACGCTGCTGATTGAGCTGGAATATTGTAATGGAGGGAACCTGTATGACAAAATC  
CTTCGTCAGAAGGACAAGTTGTTTGAGGAAGAGATGGTGGTGTGGTACCTATTTAGATT  
GTTTCAGCAGTGAGCTGCATCCATAAAGCTGGAATCCTTCATAGAGATATAAAGACATTA  
AATATTTTTCTGACCAAGGCAAACCTGATAAACTTGGAGATTATGGCCTAGCAAAGAAA  
CTTAATTCTGAGTATTCCATGGCTGAGACGCTTGTGGGAACCCCATATTACATGTCTCCA  
GAGCTCTGTCAAGGAGTAAAGTACAATTTCAAGTCTGATATCTGGGCAGTTGGCTGCGTC  
ATTTTTGAACTGCTTACCTTAAAGAGGACGTTTGTATGCTACAAACCACTTAACCTGTGT  
GTGAAGATCGTGCAAGGAATTCGGGCCATGGAAGTTGACTCTAGCCAGTACTCTTTGGAA  
TTGATCCAAATGGTTCATTTCGTGCCTTGACCAGGATCCTGAGCAGAGACCTACTGCAGAT  
GAACTTCTAGATCGCCCTCTTCTCAGGAAACGCAGGAGGTCAAGCACTGTGACTGAAGCA  
CCCATTGCTGTAGTAACATCACGAACCACTGAAGTCTATGTTTGGGGTGGTGGAAAATCC  
ACCCCCAGAACTGGATGTTATCAAGAGTGGCTGTAGTGCCCGGCAGGTCTGTGCAGGG  
AATACCCACTTTGCTGTGGTCACAGTGGAGAAGGAAGTGTACACTTGGGTGAACATGCAA  
GGAGGCACTAACTCCATGGTCAGCTGGGCCATGGAGACAAAGCCTCCTATCGACAGCCA  
AAGCATGTGGAAGAGTTGCAAGGCAAAGCTATCCGTGAGGTGTATGTGGTGATGATTTTC



## FIGURE 2HHHH

ACTGTCTGTGTGACTGATGAGGGTCAGCTCTATGCCTTCGGATCAGATTATTATGGCTGC  
ATGGGGGTGGACAAAGTTGCTGGCCCTGAAGTGCTAGAACCCATGCAGCTGAACTTCTTC  
CTCAGCAATCCAGTGGAGCAGGTCTCCTGTGGAGATAATCATGTGGTGGTTCTGACACGA  
AACAAGGAAGTCTATTCTTGGGGCTGTGGCGAATATGGACGACTGGGTTTGGATTTCAGAA  
GAGGATTATTATACACCACAAAAGGTGGATGTTCCCAAGGCCTTGATTATTGTTGCAGTT  
CAATGTGGCTGTGATGGGACATTTCTGTTGACCCAGTCAGGCAAAGTGCTGGCCTGTGGA  
CTCAATGAATTCAATAAGCTGGGTCTGAATCAGTGCATGTCGGGAATTATCAACCATGAA  
GCATACCATGAAGTTCCTACACAACGTCCTTTACCTTGGCCAAACAGTTGTCCTTTTAT  
AAGATCCGTACCATTGCCCCAGGCAAGACTCACACAGCTGCTATTGATGAGCGAGGCCGG  
CTGCTGACCTTTGGCTGCAACAAGTGTGGGCAGCTGGGCGTTGGGAACAACAAGAGCGT  
CTGGGAATCAACCTGTTGGGGGGACCCCTTGGTGGGAAGCAAGTGATCAGGGTCTCCTGC  
GGTGATGAGTTTACCATTGCTGCCACTGATGAGAAAGTATTGAATTCTAAGACCATCCGT  
TCCAATAGCAGTGGCTTATCCATTGGAAGTGTGTTTCAGAGCTCTAGCCCGGGAGGAGGC  
GGCGGGGGCGGCGGTGGTGAAGAAGAGGACAGTCAGCAGGAATCTGAACTCCTGACCCA  
AGTGAGAGGCTTCCGAGGAACAATGGAAGCAGACCGAGGAATGGAAGGTTTAATCAGTCCC  
ACAGAGGCCATGGGGAACAGTAATGGGGCCAGCAGCTCCTGTCCTGGCTGGCTTCGAAAG  
GAGCTGGAATAATGCAGAAATTTATCCCCATGCCTGACAGCCCATCTCCTCTCAGTGCAGCG  
TTTTCAGAATCTGAGAAAGATACCCTGCCCTATGAAGAGCTGCAAGGACTCAAAGTGGCC  
TCTGAAGCTCCTTTGGAACACAAACCCCAAGTAGAAGCCTCGGTAAGTGAAGCTTTTGGC  
TTTGAATCACAACCTAGTCACCTCGGCTGAATCCTGCAGTAACCTGTGCTGGGAAGGGAAC  
ACCACTGACTCCTCCTGCGTGTGCGTGCAGCTCTCTGCAGGTGGAGGTTGA

SEQ ID NO: 114\_R86668\_H, MKK6\_H

ATGAACTTGCTGCTCTCCTACGCGATGTGCAGGACTACTCGGCCATCATTGAGCTGGTG  
GAGACGCTGCAGGCCCTTGCCACCTGTGATGTGGCCGAGCAGCATAATGTCTGCTTCCAC  
TACACTTTTGCCCTCAACCGGAGGAACAGGCCTGGGGACCGGGCGAAGGCCCTGTCTGTG  
CTGCTGCCGCTGGTACAGCTTGAGGGCTCTGTGGCGCCCGATCTGTACTGCATGTGTGGC  
CGTATCTACAAGGACATGTTCTTCAGCTCGGGTTTCAGGATGCTGGGCACCGGGAGCAG  
GCCTATCACTGGTATCGCAAGGCTTTTGACGTAGAGCCAGCCTTCACTCAGGCATCAAT  
GCAGCTGTGCTCCTCATTGCTGCCGGGCAGCACTTTGAGGATTCCAAAGAGCTCCGGCTA  
ATAGGCATGAAGCTGGGCTGCCTGCTGGCCCCGAAAGGCTGCGTGGAGAAGATGCAGTAT  
TACTGGGATGTGGGTTTCTACCTGGGAGCCCAGATCCTCGCCAATGACCCACCCAGGTG  
GTGCTGGCTGCAGAGCAGCTGTATAAGCTCAATGCCCCCATATGGTACCTGGTGTCCGTG  
ATGGAGACCTTCTGCTCTACCAGCACTTCAGGCCCACGCCAGAGCCCCCTGGAGGGCCA  
CCACGCCGTGCCACTTCTGGCTCCACTTCTTGCTACAGTCCTGCCAACCATTCAGACA  
GCCTGTGCCAGGGCGACCAAGTGTGCTGGTCTGGAGATGAACAAGGTGCTGCTG  
CCTGCAAAGCTCGAGGTTGGGGTACTGACCCAGTAAGCACAGTGACCCTGAGCCTGCTG  
GAGCCTGAGACCCAGGACATTCCCTCCAGCTGGACCTTCCCAGTCGCCTCCATATGCGGA  
GTCAGCGCCTCAAAGCGCGACGAGCGCTGCTGCTTCTCTATGCACTCCCCCGGCTCAG  
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GCCTGGGTGACGAACCCGGATTCCACGGCGCCCGCGGAGGAGGCGGAGGGCGCGGGGGAG  
ATGTTGGAGTTTGATTATGAGTACACGGAGACGGGCGAGCGGCTGGTGCTGGGCAAGGGC  
ACGTATGGGGTGGTGTACGCGGGCCGCGATCGCCACACGAGGGTGCGCATCGCCATCAAG  
GAGATCCCGGAGCGGGACAGCAGGTTCTCTCAGCCCCCTGCATGAAGAGATCGCTCTTCAC  
AGACGCCTGCGCCACAAGAACATAGTGCCTATCTGGGCTCAGCTAGCCAGGGCGGCTAC  
CTTAAGATCTTCATGGAGGAAGTGCTGGAGGCAGCCTGTCTCCTTGTGCTGCGGTGCGTG  
TGGGGACCCCTGAAGGACAACGAGAGCACCATCAGTTTCTACACCCGCCAGATCCTGCAG  
GGACTTGGCTACTTGCACGACAACCACATCGTGCACAGGGACATAAAAGGGGACAATGTG  
CTGATCAACACCTTCAGTGGGCTGCTCAAGATTTCTGACTTCGGGCACCTCCAAGCGGCTG  
GCAGGCATCACACCTTGCACTGAGACCTTCACAGGAACCTCTGCAGTATATGGCCCCAGAA



## FIGURE 2IIII

ATCATTGACCAGGGCCACGCGGGTATGGGAAAGCAGCTGACATCTGGTCACTGGGCTGC  
ACTGTCATTGAGATGGCCACAGGTCGCCCCCCTTCCACGAGCTCGGGAGCCACAGGCT  
GCCATGTTTCAGGTGGGTATGTACAAGGTCCATCCGCCAATGCCAGCTCTCTGTGCGCC  
GAGGCCCAAGCCTTTCTCCTCCGAACTTTGTAGCCAGACCCCGCCTCCGAGCCAGCGCC  
CAGACACTGCTGGGGGACCCCTTCTCCTGCAGCCTGGGAAAAGGAGCCGAGCCCCAGCTCC  
CCACGACATGCTCCACGGCCCTCAGATGCCCCTTCTGCCAGTCCCACTCCTTCAGCCAAC  
TCAACCACCCAGTCTCAGACATTCCCGTGCCCTCAGGCACCCCTCTCAGCACCCACCCAGC  
CCCCCGAAGCGCTGCCTCAGTTATGGGGGCACCAGCCAGCTCCGGGTGCCCGAGGAGCCT  
GCGGCCGAGGAGCCTGCGTCTCCGGAGGAGAGTTGCGGGCTGAGCCTGCTGCACCAGGAG  
AGCAAGCGTCGGGCCATGCTGGCCGCAGTATTGGAGCAGGAGCTGCCAGCGCTGGCGGAG  
AATCTGCACCAGGAGCAGAAGCAAGAGCAGGGGGCCCGTCTGGGCAGAAACCATGTGGAA  
GAGCTGCTGCGCTGCCTCGGGGCACACATCCACACTCCCAACCGCCGGCAGCTCGCCCAG  
GAGCTGCGGGCGCTGCAAGGACGGCTGAGGGCCAGGGCCTTGGGCCTGCGCTTCTGCAC  
AGACCGCTGTTTGCTTCCCGGATGCGGTGAAGCAGATCCTCCGCAAGCGCCAGATCCGT  
CCACACTGGATGTTGCTTCTGGACTCACTGCTCAGCCGTGCTGTGCGGGCAGCCCTGGGT  
GTGCTAGGACCGGAGGTGGAGAAGGAGGCGGTCTCACCGAGGTGAGAGGAGCTGAGTAAT  
GAAGGGGACTCCAGCAGAGCCCAGGCCAGCAGAGCCCGCTTCCGGTGAGCCCGAGCAG  
GGCCCCGCTCCTCTGATGGTGCAGCTGAGCCTCTTGAGGGCAGAGACTGATCGGCTGCGC  
GAAATCCTGGCGGGGAAGGAACGGGAGTACCAGGCCCTGGTGCAGCGGGCTCTACAGCGG  
CTGAATGAGGAAGCCCGGACCTATGTCTGGCCCCAGAGCCTCCAAGTCTCTTTCAACG  
GACCAGGGCCTGGTGCAGTGGCTACAGGAAGTGAATGTGGATTGAGGCACCATCCAAATG  
CTGTTGAACCATAGCTTACCCCTCCACACTCTGCTCACCTATGCCACTCGAGATGACCTC  
ATCTACACCCGCATCAGGGGAGGGATGGTATGCCGCATCTGGAGGGCCATCTTGGCACAG  
CGAGCAGGATCCACACCAGTCACCTCTGGACCCTGA

SEQ ID NO: 115\_PAK6\_H

ATGTTTGGGAAGAAAAAGAAAGATTGAAATATCTGGCCCGTCCAACCTTTGAACACAGG  
GTTCACTACTGGGTTTGATCCACAAGAGCAGAAGTTTACCGGCCTTCCCCAGCAGTGGCAC  
AGCCTGTTAGCAGATACGGCCAACAGGCCAAAGCCTATGGTGGACCCTTCATGCATCACA  
CCCATCCAGCTGGCTCCTATGAAGACAATCGTTAGAGGAAACAAACCCTGCAAGGAAACC  
TCCATCAACGGCCTGCTAGAGGATTTTGACAACATCTCGGTGACTCGCTCCAACCTCCCTA  
AGGAAAGAAAGCCCACCCACCCAGATCAGGGAGCCTCCAGCCACGGTCCAGGCCACGCG  
GAAGAAAATGGCTTCATCACCTTCTCCCAGTATTCCAGCGAATCCGATACTACTGCTGAC  
TACACGACCGAAAAGTACAGGGAGAAGAGTCTCTATGGAGATGATCTGGATCCGTATTAT  
AGAGGCAGCCACGCAGCCAAGCAAAATGGGCACGTAATGAAAATGAAGCACGGGGAGGCC  
TACTATTCTGAGGTGAAGCCTTTGAAATCCGATTTTGCCAGATTTTCTGCCGATTATCAC  
TCACATTTGGACTCACTGAGCAAACCAAGTGAATACAGTGACCTCAAGTGGGAGTATCAG  
AGAGCCTCGAGTAGCTCCCCCTCTGGATTATTCAATTCCAATTCACACCTTCTAGAAGTGA  
GGGACCAGCGGTGCTCCAAGGAGAGCCTGGCGTACAGTGAAAGTGAATGGGGACCCAGC  
CTGGATGACTATGACAGGAGGCCAAAGTCTTCGTACCTGAATCAGACAAGCCCTCAGCCC  
ACCATGCGGCAGAGGTCCAGGTGAGGCTCGGGACTCCAGGAACCGATGATGCCATTTGGA  
GCAAGTGCAATTTAAACCCATCCCCAAGGACACTCCTACAACTCCTACACCTACCCCTCGC  
TTGTCCGAGCCCAATGTGCATTCCAAAGGTGGATTACGATCGAGCACAGATGGTCTCTC  
AGCCCTCCACTGTCAGGGTCTGACACCTACCCAGGGGCCCTGCCAACTACCTCAAAGT  
CAAAGCAAATCGGGCTATTCCCTCAAGCAGTCACCAAGTACCCGTCTGGGTACCACAAAGCC  
ACCTTGTAACCATACCCCTCCCTGCAGAGCAGTTTCGAGTACATCTCCACGGCTTCCTAC  
CTGAGCTCCCTCAGCCTCTCATCCAGCACCTACCCGCCGCCAGCTGGGGCTCCTCCTCC  
GACCAGCAGCCCTCCAGGGTGTCCCATGAACAGTTTCGGGCGGCCCTGCAGCTGGTGGTC  
AGCCCAGGAGACCCAGGGAATACTTGCCAACTTTATCAAAATCGGGGAAGGCTCAACC  
GGCATCGTATGCATCGCCACCGAGAAACACACAGGGAAACAAGTTGCAGTGAAGAAAATG

## FIGURE 2JJJJ

GACCTCCGGAAGCAACAGAGACGAGAACTGCTTTTCAATGAGGTCGTGATCATGCGGGAT  
TACCACCATGACAATGTGGTTGACATGTACAGCAGCTACCTTGTGCGGCGATGAGCTCTGG  
GTGGTCATGGAGTTTCTAGAAGGTGGTGCCTTGACAGACATTGTGACTCACACCAGAATG  
AATGAAGAACAGATAGCTACTGTCTGCCTGTCAAGTTCTGAGAGCTCTCTCCTACCTTCAT  
AACCAAGGAGTGATTACAGGGACATAAAAAAGTGAATCCATCCTCCTGACAAGCGATGGC  
CGGATAAAGTTGTCTGATTTTGGTTTCTGTGCTCAAGTTTCCAAAGAGGTGCCGAAGAGG  
AAATCATTGGTTGGCACTCCCTACTGGATGGCCCCTGAGGTGATTTCTAGGCTACCTTAT  
GGGACAGAGGTGGACATCTGGTCCCTCGGGATCATGGTGATAGAAATGATTGATGGCGAG  
CCCCCTACTTCAATGAGCCTCCCTCCAGGCGATGCGGAGGATCCGGGACAGTTTACCT  
CCAAGAGTGAAGGACCTACACAAGGTTTCTTCAAGTGCTCCGGGGATTCTTAGACTTGATG  
TTGGTGAGGGAGCCCTCTCAGAGAGCAACAGCCCAGGAATCCTCGGACATCCATTCTTA  
AACTAGCAGGTCCACCGTCTTGCATCGTCCCCCTCATGAGACAATACAGGCATCACTGA

SEQ ID NO: 116\_SURTK106\_H

ATGAATGATAGGAATGAGATTCAAATGGAAGCCAACTCCAAAGTCTTACCATTATAGCA  
CAGGAAATTCTATGCAGATTCTTTATTACCCTTAGGAGACATGCACGTTTCTTGCTCACT  
AACTAGGAAGGCAAGGAATGGCAAGGTGAGGAATTAATCACAGCTGTGCTGTGTCATT  
CTCTGTGGGCCTAGCAGGGAAGGGACAGCCCTGTGGCAATGGGCATGACACGGATGCTC  
CTGGAATGCAGTCTCAGTGACAAGTTGTGTGTCATCCAGGAGAAGCAGTATGAAGTGATT  
ATCGTCCCAACTTTGTTGGTTACTATCTTCTCATCCTTCTTGGGGTCATCCTGTGGCTT  
TTTATCAGAGAACAAAGAACTCAACAGCAGCGTTCTGGACCTCAAGGCATTGCCCCGTGT  
CCTCCACCTAGGGACCTAAGCTGGGAAGCAGGACATGGAGGAAATGTGGCTTTGCCACTT  
AAGGAGACATCCGTGGAAAACCTTCTGGGAGCTACCACACCTGCCCTGGCTAAGCTGCAG  
GTGCCGCGGGAGCAACTCTCTGAAGTTCTGGAGCAGATTGTCAGTGCTAGCTGTGGGCCC  
ATCTTTTCGAGCCAATATGAACACTGGGGACCCTTCTAAGCCCAAGAGTGTTATTCTCAAG  
GCTTTAAAAGAACCAGCTGGGCTCCATGAGGTACAAGATTTCTTAGGGCGAATCCAATTC  
CATCAATACCTGGGGAAACACAAAAACCTGGTGCAGCTGGAAGGCTGCTGCACTGAAAAAG  
CTGCCACTCTATATGGTGTGGAGGATGTGGCCCAGGGGACCTGCTCGGCTTTCTCTGG  
ACCTGTGCGGCGGGATGTGATGACTATGGATGGTCTTCTCTATGATCTCACAGAAAAACA  
GTATATCACATCGGAAAGCAAGTCCTTTTGGCGCTGGAATTCCTGCAGGAGAAGCATTG  
TTCCATGGGGATGTGGCAGCCAGGAATATTCTGATGCAAAGTGATCTCACTGCTAAGCTC  
TGTGGATTAGGCCTGGCTTATGAAGTTTACACCCGAGGGGCCATCTCCTCTACTCAAACC  
ATACCTCTCAAGTGGCTTGCCCCAGAACGGCTTCTCCTGAGACCTGCTAGCATCAGAGCA  
GATGTCTGGTCTTTTGGGATCCTGCTCTATGAGATGGTGACTCTAGGAGCACCACCGTAT  
CCTGAAGTCCCTCCTACCAGCATCCTAGAGCATCTCCAAAGAAGGAAAATCATGAAGAGA  
CCCAGTAGCTGCACACATAACCATGTACAGTATCATGAAGTCCTGCTGGCGCTGGCGTGAG  
GCTGACCGCCCCCTCACCTAGAGAGCTGCGCTTGCGCCTAGAAGCTGCCATTAAACTGCA  
GATGACGAGGCTGTGTTACAAGTACCAGAGTTGGTGGTACCTGAACTGTATGCAGCTGTG  
GCCGGCATCAGAGTGGAGAGCCTCTTCTACAACATATAGCATGCTTTGAAGAGTCTCGGGC  
AAGAAACATTATGCATGAGTATATGTTCTTGAATCAATTCTCTAAGAACAGAGAATG  
GTCTTTCCAGGGACACAAAGGGAGAAATGGGACATGGATTCTTGATCTTCTTTTACACA  
TTTCTCGGGAAATCTGAAATGATGCTGGATGGGACTCTACACATCCTGAGCTAAGACATA  
CTGTCAAGTCTCACTTCTGCTGTCCAGTCTTAGAAATCCTGGGTAGAAGTGGTGGACCTG  
TGCAAGGAGGTTTTAGAACTCTGCAGTATTTGTTGGGGCATGGCACAAATAAGCTCATC  
CCTCCCGTCCGAGGCTAGTTTCTCTGGAACCAATTTTATCTAGATGAAAATTTGGAA  
TGAAATGAAGGAATAGAAATCCAATAAAAGAGTTGAAGGGAAAGAAAATTTAAGGTTCTT  
CTTGCTCAGGATTACAGATATGGACCAACACCTCCTTCAAGAAAAGGTGGTAGGACACAA  
AGTTCTTCAAGTCTGAGCCCTACATGTGGGGCTGGAGGAGAACTATAACGGAAAAACCTC  
TGAGTTTCACTTAGGTATAGATAAAAGAAAGATGGTCCCTTTTATCTGATTCTGAGAC  
AGGTAAATTCTGTTTGTACTACGTTTAAATTAGAAGGTGGAGGAGTCATTTTCATGATTAA

## FIGURE 2KKKK

GAACATTCAACATGTATTGTTTCATTAAGCTAGCTTCCTAGTTCCGATTAGACTAAGGAGA  
CTAAGCCTAGAGAGTCAATGTTAGAACAGTGAAAAGAATTCTGTGTGTGTGTGTGTGTGT  
GTGTGTGTGTGCACAATAAATAGGAAATGTAGAAACCAAGCAAGAAGGCTTAGTAGCTCA  
GTCTTTAACAAGGGCTAGAAAAGAATGTAATCTGATATGGAAGGATAGCAGCTTCTAATT  
TTCAATCATCTGTTGATATACTGTGAACTTATTTTATTAAATTAATATTTATTAAATGG

SEQ ID NO: 117\_AA098024\_M

CTGCAGGAGAAGCACCTGTTTCATGGGGATGTGGCTGCCAGGAACATCCTGATCCAAAGT  
GACCTGACTCCCAAACCTTTGTTCATCTGGGCCCTGGCTTATGAAGTTCATGCCCATGGGGCC  
ATCTCCTCTGCTCGATCCAGCACCATCCCTCTCAAGTGGCTTGCTCCAGAAAGGCTTCTC  
CTGAGACCTGCAAGCATCAGGGGAGATATTTGGTCCTTTGGGATCCTGCTTTATGAGATG  
GTGACTCTAGGAGCACCAACCATACCCTGAAGTCCCTCCCACCAGCATCCTACAATATCTT  
CAGAGAAAAGAAAATCATGAAGAGACCCAGCAGCTGCTCACATGCCATGTACAACATCATG  
AAGTGCTGTTGGCGCTGGAGTGAGGACAGCCGCCCTTACTTGTTTCAGCTGCTCCAGCGC  
CTAGAAGCTGCTTCTAGATCTGCCGATGACAAGGCTGTGTTGCAAGTGCCAGAGTTGGTG  
GTGCCTGAACTGTATGCAGATGTGGCTGGCATCAGGGCAGAAAGCATTTCCTATAGCTTC  
AGTGTCTTTGAAGATGGTCCTAGACAAATGACTATATATGGGTGGAATTAGTTCCTTCA  
AGAACAGAGAGAAGGAACTTTCTGTGGCCACCAAGGGAGAAAAAAGGACATGGATCTTG  
CATCTTTCCCTAAACATTTTCTAGACATCTGAAATGCTGCTGGATGAAGCTCTACCTCT  
ACATACCATGTACTCTTGAGCTAAGAATCACCATCAATTGTAGTTTGCTTTCCAGTCCCA  
AGGGCTGAAGTATAAGTGGTGGACCGTGTCAATTCTAAAGGAGGTTTTTAAATCTGCAAT  
GATTGTAAGGGAATTAGGCAAAAGGGCTGGTCCCCTCACTCCAGGCTGGTTTACTACTG  
AAACTAGTTTTTTCTTTTCTTTTTTTTTTAAGTTAACTATTACAGAGTAAAAATAAACAG  
ATGGGCATGAATGAACACCTTCTAATTTTTTAACCATGAATTGAATATTGGAATTTCATGAG  
AAAGAAAATTCTAGGTTCTTTTGTCTAAGAGGTGTTAAGGTGAGTCAATATATCCTTCAA  
GGAAAGGCTTTGTCTCATCTATGTTGACGGGACGTAAAAGTCCTCGTCCCGTTATGAAGA  
GCTGAAGAAGATCTATAAGAAACAATACTGAGCCTTTCCTTGACTATAGATAGAAGAGCA  
TCCTTTTCATTGAACTCTGAGGCAGGTGGACCATGCATGATACTAAGTTTAATTAGAAGCA  
GGAGGAGTCATTTTCATGATTAGGAACATTGTTTCATCCCATTGTGTTGCCAGTTCCTGTAA  
GACTAAGGAGAATCAGCCTATAGAGCCAAAGCTAGAACCAGGGATAAAAAGTGTGTGTGT  
GTATAACAAATAGGAAGCATGAAAGTGCAGCAAGAAGACTTAGTAACCCAGGTGGTCATT  
AAGAGGTACAGAGAAGAAGTAATCTTATAGGAATGGATGGTAGCTTCTAATTTTTTAACCA  
TTCATTGAAATAACTGTGAAGCAACTCATTAAGTAGTATTTATTGACCAAAAGTAGACT  
TTTCAGGTGTATAGCTGCCAAAATCTCTATAATAAAGAGGCTAAAAGAAAATAAATGGGA  
GTTATTTTACTAGGAAAATTAGAGAACCTATAGTTTCCAAAAGAGATTCTTTATGTGCA  
AAATGAGATAACTCTCTACCTCACAGGGTGGTGTGAGGAACAATGAGAATATGTATTTG  
TGTATTATGTAGAATATAATATATTCTCAATAAATACTAGTTTTTCCCTTTT

SEQ ID NO: 118\_SGK2ALPHA\_H

GAAGAGGGCAGAGCCGTGCATGGGGCTGCTCCCCAGGACCTGAGCAGGAACCTGGAGTTT  
TCAGAGCTGCCTGATCATTGCTACAGAATGAACTCTAGCCCAGCTGGGACCCCAAGTCCA  
CAGCCCTCCAGGGCCAATGGGAACATCAACCTGGGGCCTTCAGCCAACCCAAATGCCAG  
CCCACGGACTTCGACTTCCTCAAAGTCATCGGCAAGGGAAGTACGGGAAGGTCTACTG  
GCCAAGCGCAAGTCTGATGGGGCGTTCTATGCAGTGAAGGTACTACAGAAAAAGTCCATC  
TTAAAGAAGAAAGAGCAGAGCCACATCATGGCAGAGCGCAGTGTGCTTCTGAAGAACGTG  
CGGCACCCCTTCCTCGTGGGCCTGCGCTACTCCTTCCAGACACCTGAGAAGCTCTACTTC  
GTGCTCGACTATGTCAACGGGGGAGAGCTCTTCTTCCACCTGCAGCGGGAGCGCCGTTTC  
CTGGAGCCCCGGGCCAGGTTCTACGCTGCTGAGGTGGCCAGCGCCATTGGCTACCTGCAC  
TCCCTCAACATCATTTACAGGGATCTGAAACCAGAGAACATTCTCTTGGACTGCCAGGGA  
CACGTGGTGTGACGGATTTTGGCCTCTGCAAGGAAGGTGTAGAGCCTGAAGACACCACA

## FIGURE 2LLLL

TCCACATTCTGTGGTACCCCTGAGTACTTGGCACCTGAAGTGCTTCGGAAAGAGCCTTAT  
GATCGAGCAGTGGACTGGTGGTGCTTGGGGGCAGTCCTCTACGAGATGCTCCATGGCCTG  
CCGCCCTTCTACAGCCAAGATGTATCCCAGATGTATGAGAACATTCTGCACCAGCCGCTA  
CAGATCCCCGAGGCGCGACAGTGGCCGCTGTGACCTCCTGCAAAGCCTTCTCCACAAG  
GACCAGAGGCAGCGGCTGGGCTCCAAAGCAGACTTTCTTGAGATTAAGAACCATGTATTC  
TTCAGCCCCATAAACTGGGATGACCTGTACCACAAGAGGCTAACTCCACCCTTCAACCCA  
AATGTGACAGGACCTGCTGACTTGAAGCATTTTGACCCAGAGTTCAACCAGGAAGCTGTG  
TCCAAGTCCATTGGCTGTACCCCTGACACTGTGGCCAGCAGCTCTGGGGCCTCAAGTGCA  
TTCTTGGGATTTTCTTATGCGCCAGAGGATGATGACATCTTGGATTGCTAGAAGAGAAGG  
ACCTGTGAACTACTGAGGCCAGCTGGTATTAGTAAGGAATTACCTTCAGCTGCTAGGAA  
GAGCGACTCAAATAACAATGGCTTCAACGAGAAGCAGGTTTATTTTTTCCAGCACATAA  
AAGAAAAATAATGTTTTCGGAGTCCAGGACTGGCAGGACAGGTCATCAGATACTCAGAGGC  
TGTATCTCTGCCCTGCCAACCTTGACAAATGGCTTCCAATGTTAGGTTTGCTACAAGATG  
GTTACTGGAGCTCTAGCTGCCTATTTTGTGTTTAGGGAAGGGAAAATGGAGGAAAGGGGA  
GAAGAGCAAAGGGCGCTTTTAAAGAGCTTTCCCAAAGCTCCCCCAATGACTTTTGCTT  
CCATCTCACTAACCACCCACCCCTACCTGGAATGGAGGCTGGGAAATGTGGCTTATTTGC  
TGGGTACGTGACTATCCCTAATAACAAAGGGGTTTTGACCCTAAGACATTAGGGGAGAAT  
GTTGGGTAGGCAGCCAGCCCTCTTTTACCATAGGGCCTCCTGGTGTGTTGGATTTTGATCT  
CAATGTGTAAAATGACAGAGATGTAAACAAGCTCATAGGGTATCAATATCTCTTATTGTTC  
TATGTTGAAAAA

SEQ ID NO: 120\_CCRK\_H

ATGGACCAGTACTGCATCCTGGGCCGCATCGGGGAGGGCGCCACGGCATCGTCTTCAAG  
GCCAAGCACGTGGAGACTGGCGAGATAATTGCCCTCAAGAAGGTGGCCCTAAGGCGGTTG  
GAAGACGGCTTCCCTAACCAGGCCCTGCGGGAGATTAAGGCTCTGCAGGAGATGGAGGAC  
AATCAGTATGTGGTACAACCTGAAGGCTGTGTTCCACACGGTGGAGGCTTTGTGCTGGCC  
TTTGAGTTCATGCTGTGCGATCTGGCCGAGGTGGTGCGCCATGCCCAGAGGCCACTAGCC  
CAGGCACAGGTCAAGAGCTACCTGCAGATGCTGCTCAAGGCTGTGCGCTTCTGCCATGCC  
AACAACATTGTACATCGGGACCTGAAACCTGCCAACCTGCTCATCAGCGCCTCAGGCCAG  
CTCAAGATAGCGGACTTTGGCCTGGCTCGAGTCTTTTCCCAGACGGCAGCCGCTCTAC  
ACACACCAGGTGGCCACCAGGTCTGTGGGCTGCATCATGGGGGAGCTGTTGAATGGGTCC  
CCCCTTTTCCCGGGCAAGAACGATATTGAACAGCTTTGCTATGTGCTTCGCATCTTGGGC  
ACCCCAAACCTCAAGTCTGGCCGGAGCTCACTGAGCTGCCGGACTACAACAAGATCTCC  
TTTAAGGAGCAGGTGCCCATGCCCTGGAGGAGGTGCTGCCTGACGTCTCTCCCCAGGCA  
TTGGATCTGCTGGGTCAATTCCTTCTTACCCTCCTCACCAGCGCATCGCAGCTTCCAAG  
GCTCTCCTCCATCAGTACTTCTTACAGCTCCCCTGCTGCCCATCCATCTGAGCTGCCG  
ATTCTCAGCGTCTAGGGGGACCTGCCCCCAAGGCCCATCCAGGGCCCCCCCCACATCCAT  
GACTTCCACGTGGACCGGCCCTTTGAGGGAGTCGCTGTTGAACCCAGAGCTGATTCGGCC  
CTTCATCCTGGAGGGGTGAGAAGTTGGCCCTGGTCCCGTCTGCCTGCTCCTCAGGACCAC  
TCAGTCCACCTGTTCTCTGCCACCTGCCTGGCTTCACCCTCCAAGGCCTCCCCATGGCC  
ACAGTGGGCCCCACACCACACCTTGCCCCCTTAGCCCTTGCGAGGGTTGGTCTCGAGGCAGA  
GGTCATGTTCCAGCCAAGAGTATGAGAACATCCAGTCGAGCAGAGGAGATTATGGCCT  
GTGCTCGGTGAGCCTTACCTTCTGTGTGCTACTGACGTACCCATCAGGACAGTGAGCTCT  
GCTGCCAGTCAAGGCCTGCATATGCAGAATGACGATGCCTGCCTTGGTGCTGCTTCCCC  
GAGTGCTGCCTCCTGGTCAAGGAGAAGTGACAGAGAGTAA

SEQ ID NO: 121\_TESK2\_H

GAATTCGCGGCCGCTCGACGCTCAGCAGAGCTACCAGCTGCCCTGTTGGCTTCGCTGGTC  
GGATCGTCCTCCTGGCCCCGCCAAACAGGCGAGCGGCCCGACTGTGGGGCATGGCAGTA  
GTCTCCTCGTTCTCCGCCGCCGCTAGCCTAGCTGAGTCGCCGGCTTCTGCGCTAGGGGCT

FIGURE 2MMMM

CCCACCGCCTCCGCAGGCTAAGGAGCCGCTGCCACCAACGAGCTGTGAGGGTTACTATGC  
TCCCTCTTTGCCGCCGTCTCCTCCTCTTGCCCGCGCAGGCACCCCTCTGGCTGCTCAGTC  
CTGCCTCAGTGTCAAACCAGAAGAGAAGTAAATTCACAAAAATTTATGTGTGGAGTTC  
CTTCTTAAAAGAAGAAAAAAGTGATTATTTAGACTATGGATCGGAGCAAACGGAATTCAA  
TTGCAGGATTTCTCCACGTGTGGAGCGTCTTGAAGAGTTTGAAGGAGGTGGTGGAGGAG  
AAGGAAATGTGAGCCAGGTGGGAAGAGTTTGGCCATCTTCGTATCGAGCTCTTATAAGTG  
CCTTTTCCAGACTGACGCGTTTGGATGATTTACCTGTGAAAAAATAGGGTCTGGCTTCT  
TTTCTGAAGTGTTCAAGGTACGACACCGAGCTTCTGGTCAGGTGATGGCTCTTAAGATGA  
ACACATTGAGCAGTAACCGGGCAAACATGCTGAAAGAAGTACAGCTCATGAATAGACTCT  
CCCATCCCAACATCCTTAGGTATATCAACTCCGGGAACCTGGAACAGTTGCTAGACAGTA  
ACCTGCATTTGCCTTGGACTGTGAGGGTAAAACCTGGCCTATGACATAGCAGTGGGCCTCA  
GCTACCTTCACTTCAAAGGCATTTTTTCATCGGGACCTCACATCTAAGAACTGCCTGATAA  
AGAGGGATGAGAATGGTTACTCTGCAGTGGTAGCTGACTTTGGCCTGGCTGAGAAGATCC  
CCGATGTCAGCATGGGGAGTGAGAAGCTGGCCGTGGTGGGTTCCCCATTCTGGATGGCAC  
CTGAGGTTCTCCGAGATGAGCCCTATAATGAAAGGCAGATGTGTTCTCTTATGGTATCA  
TCCTCTGCGAGATCATCGCCCGCATCCAGGCCGATCCGGACTATCTTCCCCGCACAGAGA  
ATTTCTGGGCTGGACTATGATGCTTTCCAGCACATGGTGGGAGACTGTCCCCCAGATTTTC  
TGCAACTTACTTTCAACTGCTGTAACATGGATCCCAAACCTGCGCCCATCTTTTGTGGAGA  
TTGGGAAGACCCTGGAGGAAATCTGAGCCGCCTACAGGAAGAAGAGCAGGAGAGGGATA  
GGAAGCTGCAGCCACAGCCAGGGGACTCTTGGAGAAAGCACCTGGGGTGAAGCGACTAA  
GCTCACTGGATGACAAGATCCCCCAAGTCACCATGCCCAAGACGTACCATCTGGCTGT  
CTCGAAGCCAGTCAGATATCTTTTCCCGTAAGCCCCACGTACAGTGAGTGTCTTGGACC  
CATACTACCGGCCACGAGATGGTGCTGCCCGCACCCCCAAAGTCAACCCTTTTAGTGCTC  
GCCAGGACCTCATGGGGGGCAAGATCAAGTTTTTTGACCTGCCCAGCAAGTCTGTCTCT  
CTCTGGTATTTGACCTGGATGCACCAGGGCCCGGAACTATGCCCTGGCTGACTGGCAGG  
AGCCCCGGCCCCACCTATTCGCCGGTGGCGTTCTTGCTGGTTCGCCTGAGTTCTTGC  
ATCAAGAGGCTTGTCATTTGTGGGCCGGGAAGAATCGCTATCTGATGGGCCCCCACCAC  
GCCTAAGTAGTCTCAAGTACAGAGTTAAAGAGATCCCACCATTCCGGGCATCTGCCCTAC  
CAGCTGCTCAAGCCCATGAGGCTATGGACTGCTCCATTCTCCAGGAAGAAAATGGTTTTG  
GGTCCAGGCCCCAGGGGACCAGTCCATGCCCTGCGGGTGCTTCTGAGGAGATGGAGGTAG  
AAGAAAGGCCAGCAGGCTCAACTCCAGCCACCTTCTCCACCTCAGGCATAGGCCTGCAAA  
CCCAGGGAAAGCAGGATGGGTGAGGGGGTTTAGTCCCTGCCTCACCTTGGGGATGGACCT  
TCAGCTGAAACCATATGGCCCCCTAGGTGCACAGCCTTGATTCTTCCCTGGAGCCTACAG  
AGCAGGCAGGCTAGGCCAAGCCAGGCTCAACTTCTGGGCTCCCAGTGCCCATTTGGCTGTG  
TATGACGGGAGGCAGCAGTGAGAGGCCTTCTAGTTAGGGCCAACAGCTGATACCAAGCC  
TCTGAAATCCAGCAAGGAGGTCTGCCTCCCACCAGACCCTCTCCAGTGTAATTTCCCCAGA  
TAGGACCAGAGGATGTCTAGTTCTAGGCTGAGCTGGCAGGCAGCTATTACCCCGGTTCTT  
TCCCCACCCAGGTCTGTCTCTTGCCTTTTCTTGGGGCATATAAGCTACTGAGTGGAACA  
TGGAGCTGATCAAGAGGCCGTAATGGTCATGGCTGTTTCCAGACCTGAATATTGGGTGCT  
TCTTGCCAGTATTCTAAGACATTTGAGTAATTGCTGTTTGCACCTTACTGCATGGTCAGAC  
CACGTCATACTATTTCTATGCAAGGGGACAGCAAGGCAGCGTGGTGGTTCATGGCTCTTAG  
CTAACCTATTCAAAGACCTTTTCTGTGATTAATCTATTTTCATATTTATAAAGGAGTC  
TTAATGTTCTGCCCCATAAGACTTTCAACCTTGTGGTTGGGAGTGGGGCTGGTTTTGTAG  
GCCCTAGGGCCTGCTTCTATGTATTTATCAACATGTGATACATTCAATTGGTTAAATGGT  
TTATACAGGGACTGATTTGCTTCCCTTCTGCCATGGCTGGAGCTTTGGGAACAGTCTGT  
CCTTACAGAGCTGCAATAAGAAATAACCAAAGATGAAGCTGGTCAAATATTTTCATAACT  
TGCTTCTGTTGATTTTTTTTTTTGTAAAACCTTCCCAAGACATTTTCAGACTTAAAAATAA  
AGTCAGTGTTACAGGT

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(54) Title: **PROTEIN KINASES**

(57) Abstract: The present invention relates to kinase polypeptides, nucleotide sequences encoding the kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/14842

## A. CLASSIFICATION OF SUBJECT MATTER

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A61K38/00 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, EMBL, MEDLINE, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! accession number W65887, 12 June 1996 (1996-06-12) MARRA M. ET AL.: "The WashU-HHMI mouse EST project." XP002157499 abstract DOC. AGAINST INV. 1 (SEQ.IDs. 122, 4) ---	2,6,7, 11,12
E	WO 00 58473 A (CURAGEN CORP.; LEACH MARTIN (US); SHIMKETS RICHARD A (US)) 5 October 2000 (2000-10-05) SEQ.IDs. 4435 and 4436 DOC. AGAINST INV. 1 (SEQ.IDs. 122, 4) SEQ.IDs. 5049, 5050, 5571, 5572 DOC. AGAINST INV. 67 (SEQ.IDs. 188, 70) SEQ.IDs. 3009 and 3010 DOC. AGAINST INV. 76 (SEQ.IDs. 197, 79) --- -/--	1,2,4-7, 11,12



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\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*S\* document member of the same patent family

Date of the actual completion of the international search

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>RUIZ-PEREZ V. L. ET AL.: "Mutations in a new gene in Ellis-van Creveld syndrome and Weyers acrodermal dysostosis."  NATURE GENETICS,  vol. 24, no. 3, March 2000 (2000-03),  pages 283-286, XP002157498  ISSN: 1061-4036  page 284, left-hand column, line 6 - line 8  figure 1A  page 286, right-hand column, last paragraph  &amp; DATABASE EMBL 'Online!  Accession Number Q9NY57,  1 October 2000 (2000-10-01)  RUIZ-PEREZ V. V. ET AL.: "Serine/threonine protein kinase."  abstract  DOC. AGAINST INV. 1 (SEQ.IDs. 122, 4)</p>	1-12
X	<p>DATABASE EMBL 'Online!  Accession Number AA305176,  18 April 1997 (1997-04-18)  ADAMS M. D. ET AL.: "EST176172 colon carcinoma cell line II Homo sapiens cDNA 5'-end."  XP002165842  abstract  DOC. AGAINST INV. 3 (SEQ.IDs. 124, 6)</p>	6,7
X	<p>DATABASE EMBL 'Online!  Accession Number AA116841,  16 November 1996 (1996-11-16)  MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:538568 5' similar to TR:G406058 protein kinase."  XP002165843  abstract  DOC. AGAINST INV. 4 (SEQ.IDs. 125, 7)</p>	1,2,4,6, 7,10-13, 15
P,X	<p>WO 00 06728 A (INCYTE PHARMA INC ; PATTERSON CHANDRA (US); AZIMZAI YALDA (US); COR) 10 February 2000 (2000-02-10)    SEQ.ID.1 and 32  DOC. AGAINST INV. 4 (SEQ.IDs. 125, 7)</p>	2,4-7,9, 11-14, 26,27, 35,36
X	<p>WO 98 58052 A (INCYTE PHARMA INC ; CORLEY NEIL C (US); BANDMAN OLGA (US); GOLI SUR) 23 December 1998 (1998-12-23)  SEQ.IDs. 4 and 11  DOC. AGAINST INV. 5 (SEQ.IDs. 126, 8)</p>	1-14, 26-30, 35-38
	-/--	



## INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	<p>WO 00 55332 A (INCYTE PHARMA INC ;AZIMZAI YALDA (US); YUE HENRY (US); AU YOUNG JA)  21 September 2000 (2000-09-21)  SEQ.IDs. 7 and 21  DOC. AGAINST INV. 6 (SEQ.IDs. 127, 9)  SEQ.IDs. 2 and 16  DOC. AGAINST INV. 26 (SEQ.IDs. 147, 29)  ---</p>	1-15, 26-30, 35-38
X	<p>DATABASE EMBL 'Online!  Accession Number AA593989,  24 September 1997 (1997-09-24)  STRAUSBERG R.: "Homo sapiens clone  IMAGE:1084047 3' similar to TR:G20878  serine/threonine protein kinase."  XP002165844  abstract  DOC. AGAINST INV. 6 (SEQ.IDs. 127, 9)  ---</p>	1,2,4,6, 7,10-13, 15
X	<p>DATABASE EMBL 'Online!  Accession Number AL050147,  20 May 1999 (1999-05-20)  WAM BUTT R. ET AL.: "Homo sapiens mRNA."  XP002165845  abstract  DOC. AGAINST INV. 6 (SEQ.IDs. 127, 9)  ---</p>	6,7
X	<p>HAYASHI A. ET AL.: "PKC<math>\eta</math>, a new member  of the protein kinase C family, composes a  fourth subfamily with PKC<math>\mu</math>."  BIOCHIMICA ET BIOPHYSICA ACTA,  vol. 1450, no. 1, 6 May 1999 (1999-05-06),  pages 99-106, XP000992627  ISSN: 0006-3002  the whole document  DOC. AGAINST INV. 8 (SEQ.IDs. 129, 11)  ---</p>	1-15, 35-38
X	<p>DATABASE EMBL 'Online!  Accession Number AA763046,  28 January 1998 (1998-01-28)  MARRA M. ET AL.: "Mus musculus cDNA clone  similar to TR:P70268 protein kinase."  XP002165846  abstract  DOC. AGAINST INV. 9 (SEQ.IDs. 130, 12)  ---</p>	2,6,7, 11,12
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P,X	OISHI K. ET AL.: "Identification and characterization of PKNbeta, a novel isoform of protein kinase PKN: Expression and arachidonic acid dependency are different from those of PKNalpha." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 261, no. 3, 11 August 1999 (1999-08-11), pages 808-814, XP002165839 ISSN: 0006-291X figure 1 DOC. AGAINST INV. 9 (SEQ.IDs. 130, 12) ---	1-15,26, 27,35,37
X	DATABASE EMBL 'Online! Accession Number H19102, 2 July 1995 (1995-07-02) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:171993 5' similar to SP:F31E3.2 CE01267 protein kinase." XP002165847 abstract DOC. AGAINST INV. 11 (SEQ.IDs. 132, 14) ---	2,6,7, 11,12
X	WO 97 33909 A (CORIXA CORP) 18 September 1997 (1997-09-18)  SEQ.IDs.6 and 16 DOC. AGAINST INV. 12 (SEQ.IDs. 133, 15) ---	2,6,7,9, 11,12, 26,27, 35-38
X	DATABASE EMBL 'Online! Accession Number AA463334, 13 June 1997 (1997-06-13) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:811660 5' similar to SW:COT1_NEUCR P38679 serine/threonine-protein kinase COT-1." XP002165848 abstract DOC. AGAINST INV. 12 (SEQ.IDs. 133, 15) ---	1,2,4,6, 7,10-13, 15
P,X	WO 99 57144 A (INCYTE PHARMA INC ;PATTERSON CHANDRA (US); AZIMZAI YALDA (US); RED) 11 November 1999 (1999-11-11)  SEQ.IDs. 52 and 117 DOC. AGAINST INV. 12 (SEQ.IDs. 133, 15) --- -/--	2,6,7,9, 11,12, 26,27, 29,30, 35-38

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X	DATABASE EMBL 'Online! Accession Number AC006530, 8 February 1999 (1999-02-08) ROWEN L. ET AL.: "Sequencing of human chromosome 14." XP002165849 abstract DOC. AGAINST INV. 14 (SEQ.IDs. 135, 17) ---	1,2,4-7, 10-15
X	DATABASE EMBL 'Online! Accession Number AI215680, 23 October 1998 (1998-10-23) STRAUSBERG R.: "Homo sapiens cDNA clone IMAGE:1884219." XP002165850 abstract DOC. AGAINST INV. 14 (SEQ.IDs. 135, 17) ---	6,7
X	WO 98 11234 A (HAWKINS PHILLIP R ; INCYTE PHARMA INC (US); AU YOUNG JANICE (US); G) 19 March 1998 (1998-03-19) SEQ.IDs. 5 and 6 DOC. AGAINST INV. 15 (SEQ.IDs. 136, 18) DOC. AGAINST INV. 16 (SEQ.IDs. 137, 19) ---	1-15, 26-30, 35-38
X	EP 0 861 896 A (DADE BEHRING MARBURG GMBH) 2 September 1998 (1998-09-02)  SEQ.IDs. 1 and 2 DOC. AGAINST INV. 15 (SEQ.IDs. 136, 18) DOC. AGAINST INV. 16 (SEQ.IDs. 137, 19) ---	1-15, 26-28, 35-38
P,X	DATABASE EMBL 'Online! Accession Number AF205855, 23 December 1999 (1999-12-23) SHIGAEV A. ET AL.: "Mus musculus serum and glucocorticoid-dependent protein kinase (Sgk) mRNA." XP002165851 abstract DOC. AGAINST INV. 16 (SEQ.IDs. 137, 19) ---	1,2,4,6, 7,10-13, 15

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E	WO 00 35946 A (UNIV DUNDEE ;COHEN PHILIP (GB); DEAK MARIA (GB); KOBAYASHI TAKAYAS) 22 June 2000 (2000-06-22) figure 11 DOC. AGAINST INV. 17 (SEQ.IDs. 138, 20) DOC. AGAINST INV. 113 (SEQ.IDs. 234, 116) ---	1-14, 26, 27, 29, 30
X	DATABASE EMBL 'Online! Accession Number Z98752, 23 August 1997 (1997-08-23) RAMSAY H.: "Human DNA sequence from clone RP1-138B7 on chromosome 20q13.12." XP002165852 abstract DOC. AGAINST INV. 17 (SEQ.IDs. 138, 20) ---	1-14
X	WO 98 31802 A (GENETICS INST) 23 July 1998 (1998-07-23) SEQ.IDs. 13 and 14 DOC. AGAINST INV. 21 (SEQ.IDs. 142, 24) ---	6, 7, 11, 12
X	DATABASE EMBL 'Online! Accession Number AI061003, 23 July 1998 (1998-07-23) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:1379597 5' similar to TR:008875 calcium calmodulin dependent kinase CPG16." XP002165853 abstract DOC. AGAINST INV. 22 (SEQ.IDs. 143, 25) ---	1, 2, 4, 6, 7, 10-13, 25
X	DATABASE EMBL 'Online! Accession Number AA383293, 18 April 1997 (1997-04-18) ADAMS M. D. ET AL.: "Homo sapiens cDNA 5'-end similar to serine/threonine kinase p78." XP002165854 abstract DOC. AGAINST INV. 23 (SEQ.IDs. 144, 26) ---	1, 2, 4, 6, 7, 10-13, 16
X	DATABASE EMBL 'Online! Accession number AA197883, 29 January 1997 (1997-01-29) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:654045 5' similar to TR:G406113 protein kinase I." XP002165855 abstract DOC. AGAINST INV. 24 (SEQ.IDs. 145, 27) ---	1, 2, 4, 6, 7, 10-13

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P, X	WO 99 50395 A (HELIX RESEARCH INST ;MURAMATSU MASAOKI (JP); TOKUMITSU HIROSHI (JP) 7 October 1999 (1999-10-07) page 41 -page 51 DOC. AGAINST INV. 24 (SEQ.IDs. 145, 27) ---	1-4,6-13
X	SANJO H. ET AL: "DRAKS, novel serine/threonine kinases related to death-associated protein kinase that trigger apoptosis." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 44, 30 October 1998 (1998-10-30), pages 29066-29071, XP002165841 ISSN: 0021-9258 figure 1 DOC. AGAINST INV. 26 (SEQ.IDs. 147, 29) ---	1-14,16, 35,37
P, X	WO 99 33961 A (AKIRA SHIZUO ;KAWAI TARO (JP); ASAHI CHEMICAL IND (JP)) 8 July 1999 (1999-07-08)  SEQ.IDs. 5 and 6 DOC. AGAINST INV. 26 (SEQ.IDs. 147, 29) SEQ.IDs. 29 and 30 DOC. AGAINST INV. 40 (SEQ.IDs. 161, 43) ---	1-14,16, 26,27, 29,30, 35,37
X	NAGASE T. ET AL.: "PREDICTION OF THE CODING SEQUENCE OF UNIDENTIFIED HUMAN GENES. XIII. THE COMPLETE SEQUENCE OF 100 NEW CDNA CLONES FROM BRAIN WHICH CODE FOR LARGE PROTEINS IN VITRO" DNA RESEARCH, vol. 6, 26 February 1999 (1999-02-26), pages 63-70, XP000952912 ISSN: 1340-2838 the whole document -& DATABASE EMBL 'Online! Accession Number AB023153, 9 April 1999 (1999-04-09) NAGASE T. ET AL.: "Homo sapiens mRNA for KIAA0936 protein." XP002166242 abstract DOC. AGAINST INV. 54 (SEQ.IDs. 175, 57) -& DATABASE EMBL 'Online! Accession Number AB023216, 9 April 1999 (1999-04-09) NAGASE T. ET AL.: "Homo sapiens mRNA for KIAA0999 protein." XP002166243 abstract DOC. AGAINST INV. 28 (SEQ.IDs. 149, 31) ---	1,2,4-7, 10-14, 16,19

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X	WO 98 01756 A (UNIV WASHINGTON) 15 January 1998 (1998-01-15)  SEQ.IDs. 1 and 2 DOC. AGAINST INV. 30 (SEQ.IDs. 151, 33) ---	1-14, 16, 26, 27, 35, 36
X	DATABASE EMBL 'Online! Accession Number W90839, 9 July 1996 (1996-07-09) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:420441 5' similar to gb:M80359 putative serine/threonine protein kinase." XP002165856 abstract DOC. AGAINST INV. 31 (SEQ.IDs. 152, 34) ---	1, 2, 4, 6, 7, 10-13, 16
X	NAGASE T. ET AL.: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES. IV. THE CODING SEQUENCES OF 40 NEW GENES (KIAA0121-KIAA0160) DEDUCED BY ANALYSIS OF CDNA CLONES FROM HUMAN CELL LINE KG-1" DNA RESEARCH, vol. 2, no. 4, 31 August 1995 (1995-08-31), pages 167-174, XP000676653 ISSN: 1340-2838 the whole document -& DATABASE EMBL 'Online! Accession Number D50925, 1 August 1996 (1996-08-01) NAGASE T. ET AL.: "Human mRNA for KIAA0135 gene." XP002166244 abstract DOC. AGAINST INV. 32 (SEQ.IDs. 153, 35) DOC. AGAINST INV. 33 (SEQ.IDs. 154, 36) ---	1, 2, 4-7, 10-14, 16
X	DATABASE EMBL 'Online! Accession Number U79240, 14 December 1996 (1996-12-14) YU W. ET AL.: "Human serine/threonine kinase mRNA." XP002165857 abstract DOC. AGAINST INV. 33 (SEQ.IDs. 154, 36) ---	1, 2, 4-7, 10-14
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X	<p>DATABASE EMBL 'Online!  Accession Number AI036899,  29 June 1998 (1998-06-29)  MARRA M. ET AL.: "Mus musculus cDNA clone  IMAGE:1746011 5' similar to TR:Q99763  serine/threonine protein kinase."  XP002165858  abstract  DOC. AGAINST INV. 33 (SEQ.IDs. 154, 36)</p> <p>---</p>	1,2,4,6, 7,10-13
X	<p>DATABASE EMBL 'Online!  Accession Number AI469033,  17 March 1999 (1999-03-17)  STRAUSBERG R.: "Homo sapiens cDNA clone  IMAGE:2137322."  XP002165859  abstract  DOC. AGAINST INV. 35 (SEQ.IDs. 156, 38)</p> <p>---</p>	6,7
X	<p>DATABASE EMBL 'Online!  Accession Number AC007225,  7 April 1999 (1999-04-07)  BRUCE D. ET AL.: "Homo sapiens chromosome  16 clone RPCI-11_480G7."  XP002166245  abstract  DOC. AGAINST INV. 37 (SEQ.IDs. 158, 40)</p> <p>---</p>	6,7
P,X	<p>WO 99 49062 A (FAN WUFANG ;GENE LOGIC INC  (US); PRASHAR YATINDRA (US))  30 September 1999 (1999-09-30)  SEQ.IDs. 1 and 2  DOC. AGAINST INV. 37 (SEQ.IDs. 158, 40)  DOC. AGAINST INV. 55 (SEQ.IDs. 176, 58)</p> <p>---</p>	1-14, 26-30, 35-38
X	<p>DATABASE EMBL 'Online!  Accession Number AI596766,  26 April 1999 (1999-04-26)  MARRA M. ET AL.: "Mus musculus cDNA clone  IMAGE:949322 5' similar to WP:ZC373.4  CE02377 myosin-light-chain kinase domain."  XP002166246  abstract  DOC. AGAINST INV. 38 (SEQ.IDs. 159, 41)  DOC. AGAINST INV. 39 (SEQ.IDs. 160, 42)</p> <p>---</p> <p>-/--</p>	1,2,4,6, 7,10-13, 16

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>NAGASE T. ET AL.: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES. XVI. THE COMPLETE SEQUENCES OF 150 NEW CDNA CLONES FROM BRAIN WHICH CODE FOR LARGE PROTEINS IN VITRO"</p> <p>DNA RESEARCH, vol. 7, 28 February 2000 (2000-02-28), pages 65-73, XP000923011 KIAA1297</p> <p>-&amp; DATABASE EMBL 'Online! Accession Number AB037718, 14 March 2000 (2000-03-14)</p> <p>OHARA O. ET AL.: "Homo sapiens mRNA for KIAA1297 protein." XP002166247 abstract DOC. AGAINST INV. 38 (SEQ.IDs. 159, 41) DOC. AGAINST INV. 39 (SEQ.IDs. 160, 42) -&amp; DATABASE EMBL 'Online! Accession Number AB037759, 14 March 2000 (2000-03-14)</p> <p>OHARA O. ET AL.: "Homo sapiens mRNA for KIAA1338 protein." XP002167889 abstract DOC. AGAINST INV. 67 (SEQ.IDs. 188, 70) -&amp; DATABASE EMBL 'Online! Accession Number AB037790, 14 March 2000 (2000-03-14)</p> <p>OHARA O. ET AL.: "Homo sapiens mRNA for KIAA1369 protein." XP002167890 abstract DOC. AGAINST INV. 68 (SEQ.IDs. 189, 71) -&amp; DATABASE EMBL 'Online! Accession Number AB037781, 14 March 2000 (2000-03-14)</p> <p>NAGASE T. ET AL.: "Homo sapiens mRNA for KIAA1360 protein, partial cds." XP002168226 abstract DOC. AGAINST INV. 82 (SEQ.IDs. 203, 85) ---</p>	1,2,4-7, 10-14, 16,25
X	<p>KAWAI T. ET AL.: "Duet is a novel serine/threonine kinase with Dbl-Homology (DH) and Pleckstrin-Homology (PH) domains"</p> <p>GENE, vol. 227, no. 2, 18 February 1999 (1999-02-18), pages 249-255, XP004158739 ISSN: 0378-1119 the whole document DOC. AGAINST INV. 40 (SEQ.IDs. 161, 43) ---</p> <p style="text-align: center;">-/--</p>	1-14,29, 30,35-38



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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online!  Accession Number AA454060,  11 June 1997 (1997-06-11)  HILLIER L. ET AL.: "Homo sapiens cDNA  clone IMAGE:795492 5' similar to TR:G49075  calmodulin-binding protein."  XP002166248  abstract  DOC. AGAINST INV. 41 (SEQ.IDs. 162, 44)</p> <p>---</p>	6,7
X	<p>DATABASE EMBL 'Online!  Accession Number AI385971,  29 January 1999 (1999-01-29)  MARRA M. ET AL.: "Mus musculus cDNA clone  IMAGE:514336 5' similar to WP:R90.1  CE06325 protein kinase."  XP002166249  abstract  DOC. AGAINST INV. 43 (SEQ.IDs. 164, 46)</p> <p>---</p>	1,2,4,6, 7,10-13, 16
X	<p>DATABASE EMBL 'Online!  Accession Number AA436054,  1 June 1997 (1997-06-01)  HILLIER L. ET AL.: "Homo sapiens cDNA  clone IMAGE:730582 5' similar to gb:X66363  serine/threonine-protein kinase pctaie-1"  XP002166250  abstract  DOC. AGAINST INV. 44 (SEQ.IDs. 165, 47)</p> <p>---</p>	1,2,4-7, 10-14,16
X	<p>DATABASE EMBL 'Online!  Accession Number AA061797,  24 September 1996 (1996-09-24)  MARRA M. ET AL.: "Mus musculus cDNA clone  IMAGE:513953 5' similar to gb:X66358  serine/threonine-protein kinase."  XP002166251  abstract  DOC. AGAINST INV. 45 (SEQ.IDs. 166, 48)  DOC. AGAINST INV. 46 (SEQ.IDs. 167, 49)</p> <p>---</p>	1,2,4,6, 7,10-13, 17
A	<p>WO 98 35015 A (GERHOLD DAVID L ;MERCK &amp; CO  INC (US)) 13 August 1998 (1998-08-13)  SEQ.IDs.2 and 3  DOC. AGAINST INV. 50 (SEQ.IDs. 171, 53)  DOC. AGAINST INV. 114 (SEQ.IDs. 235, 117)</p> <p>---</p> <p style="text-align: center;">-/--</p>	1-30, 35-38

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X	NAYLER O. ET AL.: "Characterization and comparison of four serine- and arginine-rich (SR) protein kinases." BIOCHEMICAL JOURNAL, vol. 326, no. 3, 1997, pages 693-700, XP002166240 ISSN: 0264-6021 the whole document DOC. AGAINST INV. 51 (SEQ.IDs. 172, 54) ---	1-4, 6-13,18, 26,27
P,X	WO 99 38981 A (AKERBLOM INGRID E ;INCYTE PHARMA INC (US); CORLEY NEIL C (US); BAN) 5 August 1999 (1999-08-05) SEQ.IDs. 3 and 9 DOC. AGAINST INV. 51 (SEQ.IDs. 172, 54) SEQ.IDs. 6 and 12 DOC. AGAINST INV. 95 (SEQ.IDs. 216, 43) ---	1-14,18, 26-30, 35-38
X	DATABASE EMBL 'Online! Accession Number AA839940, 2 March 1998 (1998-03-02) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:1259911 5' similar to SW:KMLC_RAT P20689 myosin light chain kinase." XP002167891 abstract DOC. AGAINST INV. 55 (SEQ.IDs. 176, 58) ---	1,2,4,6, 7,10-13, 18
X	DATABASE EMBL 'Online! Accession Number AL031055, 10 July 1998 (1998-07-10) RAMSAY H.: "Human DNA sequence from clone RP1-28H20 on chromosome 20q13.1." XP002167892 abstract DOC. AGAINST INV. 56 (SEQ.IDs. 177, 59) ---	1,2,4-7, 10-14,18
P,X	DATABASE EMBL 'Online! Accession Number AL137662, 27 January 2000 (2000-01-27) KOEHRER K. ET AL.: "Homo sapiens mRNA" XP002167893 abstract DOC. AGAINST INV. 57 (SEQ.IDs. 178, 60) ---	2,6,7, 11,12
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X	<p>NAGASE T. ET AL.: "Prediction of the coding sequences of unidentified human genes. VII. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro"</p> <p>DNA RESEARCH, vol. 4, no. 4, 28 April 1997 (1997-04-28), pages 141-150, XP002102085 ISSN: 1340-2838 the whole document -&amp; DATABASE EMBL 'Online! Accession Number AB002342, 1 July 1997 (1997-07-01) NAGASE T. ET AL.: "Human mRNA for KIAA0344 gene." XP002167894 abstract DOC. AGAINST INV. 59 (SEQ.IDs. 180, 62)</p>	2,6,7, 11,12
X	<p>WO 98 36054 A (HOOPER JOHN DAVID ;AMRAD OPERATIONS PTY LTD (AU); ANTALIS TONI MAR) 20 August 1998 (1998-08-20) SEQ.IDs. 9 and 10 DOC. AGAINST INV. 60 (SEQ.IDs. 181, 63)</p>	1-14, 26-30, 35-38
X	<p>ANDERSON K. A. ET AL.: "Components of a calmodulin-dependent protein kinase cascade. Molecular cloning, functional characterization and cellular localization of Ca2+/calmodulin-dependent protein kinase kinase beta."</p> <p>JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 48, 27 November 1998 (1998-11-27), pages 31880-31889, XP002167887 ISSN: 0021-9258 the whole document -&amp; DATABASE EMBL 'Online! Accession Number AF140507, 21 May 1999 (1999-05-21) ANDERSON K. A. ET AL.: "Homo sapiens Ca2+/calmodulin-dependent protein kinase beta, complete cds." XP002167895 abstract DOC. AGAINST INV. 62 (SEQ.IDs. 183, 65)</p>	1-14,23, 26,27
P,X	<p>WO 99 58558 A (INCYTE PHARMA INC ;PATTERSON CHANDRA (US); YUE HENRY (US); BANDMAN) 18 November 1999 (1999-11-18) SEQ.IDs. 2 and 15 DOC. AGAINST INV. 62 (SEQ.IDs. 183, 65)</p>	2,6,7,9, 11,12, 26-28

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X	DATABASE EMBL 'Online! Accession Number AC004685, 15 May 1998 (1998-05-15) ADAMS M. D. AND LOFTUS B. J.: "Homo sapiens chromosome 16 BAC clone CIT987SK-A-233A8." XP002167896 abstract DOC. AGAINST INV. 63 (SEQ.IDs. 184, 66) ---	1,2,4-7
P,X	US 6 013 455 A (AZIMZAI YALDA ET AL) 11 January 2000 (2000-01-11)  SEQ.IDs. 2 and 11 DOC. AGAINST INV. 63 (SEQ.IDs. 184, 66) ---	1-14, 26-30, 35-38
X	EP 0 870 825 A (SMITHKLINE BEECHAM CORP) 14 October 1998 (1998-10-14)  figure 2 DOC. AGAINST INV. 65 (SEQ.IDs. 186, 68) DOC. AGAINST INV. 66 (SEQ.IDs. 187, 69) ---	1-14, 25-30, 35-38
X	DATABASE EMBL 'Online! Accession Number AA589241, 18 September 1997 (1997-09-18) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:992145 5' similar to WP:F49E11.1 CE05897 serine/threonine protein kinase." XP002167897 abstract DOC. AGAINST INV. 66 (SEQ.IDs. 187, 69) ---	1,2,4,6, 7,10-13, 25
P,X	BERLANGA J. J. ET AL.: "Characterization of a mammalian homolog of the GCN2 eukaryotic initiation factor 2alpha kinase." EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 265, no. 2, October 1999 (1999-10), pages 754-762, XP002167888 ISSN: 0014-2956 the whole document DOC. AGAINST INV. 67 (SEQ.IDs. 188, 70) ---	1-14, 25-27,35
X	WO 94 05794 A (MASSACHUSETTS INST TECHNOLOGY) 17 March 1994 (1994-03-17)  page 13, paragraph 2 examples 1,2 DOC. AGAINST INV. 68 (SEQ.IDs. 189, 71) ---	1-14, 26-28, 35-38
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X	MELLOR H. ET AL.: "CLONING AND CHARACTERIZATION OF CDNA ENCODING RAT HEMIN-SENSITIVE INITIATION FACTOR-2ALPHA (EIF-2ALPHA) KINASE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 269, no. 14, 8 April 1994 (1994-04-08), pages 10201-10204, XP002920790 ISSN: 0021-9258 the whole document DOC. AGAINST INV. 68 (SEQ.IDs. 189, 71) ---	1-4,6-13
X	DATABASE EMBL 'Online! Accession Number AA387681, 25 June 1997 (1997-06-25) MARRA M. ET AL.: "Mus musculus cDNA clone." XP002167898 abstract DOC. AGAINST INV. 70 (SEQ.IDs. 191, 73) ---	6,7
P,X	WO 00 09678 A (TULARIK INC) 24 February 2000 (2000-02-24)  the whole document DOC. AGAINST INV. 71 (SEQ.IDs. 192, 74) ---	1-14,20, 26,27, 29,30, 35-38
X	DATABASE EMBL 'Online! Accession Number AF046653, 6 April 1998 (1998-04-06) ZAMBROWICZ B. P. ET AL.: "Mus musculus genomic clone OST10140." XP002167969 abstract DOC. AGAINST INV. 76 (SEQ.IDs. 197, 79) ---	1-4, 6-13,25
P,X	DATABASE EMBL 'Online! Accession Number AF238255, 12 April 2000 (2000-04-12) LIU T. C. ET AL.: "Homo sapiens mixed lineage kinase mRNA." XP002167970 abstract -& LIU T.-C. ET AL.: "Cloning and expression of ZAK, a mixed lineage kinase-like protein containing a leucine-zipper and a sterile-alpha motif." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 274, 11 August 2000 (2000-08-11), pages 811-816, XP002167968 the whole document DOC. AGAINST INV. 77 (SEQ.IDs. 198, 80) ---	1-14

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Int. l. Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00 14212 A (ACTON SUSAN ;MILLENNIUM PHARM INC (US)) 16 March 2000 (2000-03-16)  figure 2 DOC. AGAINST INV. 77 (SEQ.IDs. 198, 80) figure 3 DOC. AGAINST INV. 106 (SEQ.IDs. 227, 109) ---	1-14, 25-30, 35-38
X	DATABASE EMBL 'Online! Accession Number AA270784, 28 March 1997 (1997-03-28) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:736476." XP002167971 abstract DOC. AGAINST INV. 80 (SEQ.IDs. 201, 83) ---	6,7
P,X	PAZDERNIK N. J. ET AL.: "MOUSE RECEPTOR INTERACTING PROTEIN 3 DOES NOT CONTAIN A CASPASE-RECRUITING OR A DEATH DOMAIN BUT INDUCES APOPTOSIS AND ACTIVATES NF-(KAPPA)B" MOLECULAR AND CELLULAR BIOLOGY, vol. 19, no. 10, October 1999 (1999-10), pages 6500-6508, XP000939146 the whole document DOC. AGAINST INV. 80 (SEQ.IDs. 201, 83) ---	1-4, 6-13,22
X	DATABASE EMBL 'Online! Accession Number AL031297, 13 August 1998 (1998-08-13) COBLEY V.: "Human DNA sequence from clone 97P20 on chromosome1q23.2-24.3." XP002168227 abstract DOC. AGAINST INV. 81 (SEQ.IDs. 202, 84) ---	1-14
X	WO 99 04265 A (SAHIN UGUR ;TURECI OZLEM (DE); PFREUNDSCHUH MICHAEL (DE); GOUT IVA) 28 January 1999 (1999-01-28) SEQ.IDs. 431 and 435 DOC. AGAINST INV. 82 (SEQ.IDs. 203, 85) ---	2,6,7, 11,12
X	DATABASE EMBL 'Online! Accession Number AA195964, 28 January 1997 (1997-01-28) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:628136" XP002168228 abstract DOC. AGAINST INV. 84 (SEQ.IDs. 205, 87) ---	6,7

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## INTERNATIONAL SEARCH REPORT

Int. .ional Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>DATABASE EMBL 'Online!  Accession Number AK000342,  22 February 2000 (2000-02-22)  SUGANO S. ET AL.: "Homo sapiens cDNA  FLJ20335 fis, clone HEP11429."  XP002168229  abstract  DOC. AGAINST INV. 84 (SEQ.IDs. 205, 87)</p> <p>---</p>	1-14
X	<p>DATABASE EMBL 'Online!  Accession Number AF027406,  6 January 1999 (1999-01-06)  BRENNER V. ET AL.: "Homo sapiens  muscle-specific serine kinase 1 (MSSK1)  mRNA."  XP002168230  abstract  DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88)</p> <p>---</p>	1-14
X	<p>DATABASE EMBL 'Online!  Accession Number AF043288,  6 January 1999 (1999-01-06)  BRENNER V. ET AL.: "Mus musculus  muscle-specific serine kinase 1 mRNA."  XP002168231  abstract  DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88)</p> <p>---</p>	1-4, 6-13
P, X	<p>WO 00 22143 A (INCYTE PHARMA INC ;AZIMZAI  YALDA (US); CORLEY NEIL C (US); YUE HEN)  20 April 2000 (2000-04-20)  SEQ.IDs. 1 and 10  DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88)  SEQ.IDs. 7 and 16  DOC. AGAINST INV. 104 (SEQ.IDs. 225, 107)</p> <p>---</p>	1-4, 6-13, 26-28
X	<p>DATABASE EMBL 'Online!  Accession Number AI553938,  25 March 1999 (1999-03-25)  STAUSBERG R.: "Homo sapiens cDNA clone  IMAGE:2090493 3' similar to TR:015367  TSK_1."  XP002168388  abstract  DOC. AGAINST INV. 86 (SEQ.IDs. 207, 89)  DOC. AGAINST INV. 87 (SEQ.IDs. 208, 90)  DOC. AGAINST INV. 91 (SEQ.IDs. 212, 94)</p> <p>---</p> <p style="text-align: center;">-/--</p>	1, 2, 4-7, 10-14, 25

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online!  Accession Number AV040939,  14 May 1999 (1999-05-14)  CARNINCI P. ET AL.: "Mus musculus adult  male testis cDNA, partial sequence."  XP002168389  abstract  DOC. AGAINST INV. 87 (SEQ.IDs. 208, 90)  ---</p>	6,7
X	<p>DATABASE EMBL 'Online!  Accession Number AA399596,  29 April 1997 (1997-04-29)  HILLIER L. ET AL.: "Homo sapiens cDNA  clone IMAGE:729913 5' similar to  TR:G404634 Serine/threonine kinase."  XP002168766  abstract  DOC. AGAINST INV. 88 (SEQ.IDs. 209, 91)  ---</p>	1,2,4-7, 10-14,25
X	<p>KUENG P. ET AL: "A novel family of  serine/threonine kinases participating in  spermiogenesis."  JOURNAL OF CELL BIOLOGY,  vol. 139, no. 7,  29 December 1997 (1997-12-29), pages  1851-1859, XP002168387  ISSN: 0021-9525  the whole document  DOC. AGAINST INV. 89 (SEQ.IDs. 210, 92)  ---</p>	1-14, 26-28, 35-38
X	<p>DATABASE EMBL 'Online!  Accession Number AI652441,  5 May 1999 (1999-05-05)  STRAUSBERG R.: "Homo sapiens cDNA clone  IMAGE:2307063 3' similar to TR:P97417  serine/threonine kinase"  XP002168390  abstract  DOC. AGAINST INV. 89 (SEQ.IDs. 210, 92)  ---</p>	1,2,4-7, 10-14
X	<p>DATABASE EMBL 'Online!  Accession Number L77564,  16 June 1996 (1996-06-16)  GONG W. ET AL.: "Homo sapiens DGS-G mRNA,  3'-end."  XP002168391  abstract  DOC. AGAINST INV. 89 (SEQ.IDs. 210, 92)  ---</p> <p style="text-align: center;">-/--</p>	1,2,4-7, 10-14



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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online!  Accession Number AA905446,  9 April 1998 (1998-04-09)  STRAUSBERG R.: "Homo sapiens cDNA clone  IMAGE:1506197 3' similar to TR:P97417  serine threonine kinase."  XP002168767  abstract  DOC. AGAINST INV. 91 (SEQ.IDs. 212, 9)  DOC. AGAINST INV. 86 (SEQ.IDs. 207, 89)  ---</p>	1,2,4-7, 10-14,25
X	<p>DATABASE EMBL 'Online!  Accession Number AI538521,  24 March 1999 (1999-03-24)  STRAUSBERG R.: "Homo sapiens cDNA clone  IMAGE:2074994 3' similar to SW:UN51_CAEEEL  Q23023 serine/threonine protein kinase  UNC-51"  XP002168768  abstract  DOC. AGAINST INV. 92 (SEQ.IDs. 213, 95)  DOC. AGAINST INV. 93 (SEQ.IDs. 214, 96)  ---</p>	1,2,4-7, 10-14,25
X	<p>DATABASE EMBL 'Online!  Accession Number AA498104,  3 July 1997 (1997-07-03)  MARRA M. ET AL.: "Mus musculus cDNA clone  IMAGE:918101."  XP002168769  abstract  DOC. AGAINST INV. 93 (SEQ.IDs. 214, 96)  ---</p>	6,7
X	<p>DATABASE EMBL 'Online!  Accession Number AA215311,  5 February 1997 (1997-02-05)  STRAUSBERG R.: "Homo sapiens cDNA clone  IMAGE:63368 5' similar to TR:E237261  calmodulin-domain protein kinase."  XP002168770  abstract  DOC. AGAINST INV. 94 (SEQ.IDs. 215, 97)  ---</p>	1,2,4-7, 10-14
P,X	<p>WO 99 32609 A (KAROLINSKA INNOVATIONS AB  ;ZAPHIROPOULOS PETER G (SE); TOFTGAARD R)  1 July 1999 (1999-07-01)  SEQ.IDs. 1 and 2  DOC. AGAINST INV. 95 (SEQ.IDs. 216, 98)  ---</p> <p style="text-align: center;">-/--</p>	1-14,18, 26-28, 35-38

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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X	<p>DATABASE EMBL 'Online!  Accession Number AA018361,  10 August 1996 (1996-08-10)  HILLIER L. ET AL.: "Homo sapiens cDNA  clone IMAGE:361543 5' similar to  SW:ASK1_ARATH P43291 serine/threonine  kinase ASK2."  XP002169144  abstract  DOC. AGAINST INV. 95 (SEQ.IDs. 216, 98)</p> <p>---</p>	1,2,4-7, 10-14,18
X	<p>DATABASE EMBL 'Online!  Accession Number AI651075,  5 May 1999 (1999-05-05)  STRAUSBERG R.: "Homo sapiens cDNA clone  IMAGE:2304078 3' similar to TR:060679  serum inducible kinase."  XP002169145  abstract  DOC. AGAINST INV. 97 (SEQ.IDs. 218, 100)</p> <p>---</p>	1,2,4-7, 10-14,25
X	<p>DATABASE EMBL 'Online!  Accession Number W08549,  27 April 1996 (1996-04-27)  MARRA M. ET AL.: "Mus musculus cDNA clone  IMAGE:332593."  XP002169146  abstract  DOC. AGAINST INV. 98 (SEQ.IDs. 219, 101)</p> <p>---</p>	6,7
X	<p>DATABASE EMBL 'Online!  Accession Number AC002355,  24 July 1997 (1997-07-24)  HAWKINS T. L. ET AL.: "Homo sapiens  chromosome 9 clone 107G20 map 9q34"  XP002169147  abstract  DOC. AGAINST INV. 99 (SEQ.IDs. 220, 102)</p> <p>---</p>	1-7
X	<p>DATABASE EMBL 'Online!  Accession Number AI606679,  26 April 1999 (1999-04-26)  MARRA M. ET AL.: "Mus musculus cDNA clone  IMAGE:516008."  XP002169148  abstract  DOC. AGAINST INV.100 (SEQ.IDs. 221, 103)</p> <p>---</p> <p style="text-align: center;">-/--</p>	6,7

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online!  Accession Number AA493011,  2 July 1997 (1997-07-02)  MARRA. M. ET AL.: "Mus musculus cDNA clone  IMAGE:917574."  XP002169149  abstract  DOC. AGAINST INV.100 (SEQ.IDs. 221, 103)  ---</p>	6,7
X	<p>DATABASE EMBL 'Online!  Accession Number AA396601,  28 April 1997 (1997-04-28)  MARRA M. ET AL.: "Mus musculus cDNA clone  IMAGE:570118."  XP002169150  abstract  DOC. AGAINST INV.102 (SEQ.IDs. 223, 105)  ---</p>	6,7
E	<p>EP 1 033 401 A (GENSET SA)  6 September 2000 (2000-09-06)  SEQ.ID.6560  DOC. AGAINST INV.102 (SEQ.IDs. 223, 105)  ---</p>	2,6,7, 11,12
X	<p>DATABASE EMBL 'Online!  Accession Number AA276191,  3 April 1997 (1997-04-03)  MARRA M. ET AL.: " Mus musculus cDNA clone  IMAGE:776192 5' similar t .SW:KRB1_VACCC  P20505 30 KD prtein kinase homolog."  XP002169151  abstract  DOC. AGAINST INV.104 (SEQ.IDs. 225, 107)  ---</p>	1-4,6-13
X	<p>DATABASE EMBL 'Online!  Accession Number AA399022,  29 April 1997 (1997-04-29)  HILLIER L. ET AL.: "Homo sapiens cDNA  clone IMAGE:729929."  XP002169312  abstract  DOC. AGAINST INV.106 (SEQ.IDs. 227, 109)  ---</p>	6,7
X	<p>WO 97 47750 A (IMMUNEX CORP)  18 December 1997 (1997-12-18)   the whole document  DOC. AGAINST INV.108 (SEQ.IDs. 229, 111)  ---</p> <p style="text-align: center;">-/--</p>	1-14, 25-30, 35-38

## INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online!  Accession Number AI298668,  4 December 1998 (1998-12-04)  STRAUSBERG R.: "Homo sapiens cDNA clone  IMAGE:1895716 3' similar to SW:NEK1_Mouse  P51945 serine/threonine-protein kinase  NEK1."  XP002169313  abstract  DOC. AGAINST INV.108 (SEQ.IDs. 229, 111)</p>	1,2,4-7, 10-14,25
X	<p>WANG X. S. ET AL.: "MAPKKK6, a novel  mitogen-activated protein kinase kinase  kinase, that associates with MAPKKK5."  BIOCHEMICAL AND BIOPHYSICAL RESEARCH  COMMUNICATIONS,  vol. 253, no. 1,  9 December 1998 (1998-12-09), pages 33-37,  XP002169311  ISSN: 0006-291X  the whole document  DOC. AGAINST INV.109 (SEQ.IDs. 230, 112)</p>	1-14,25
X	<p>DATABASE EMBL 'Online!  Accession Number AI638161,  29 April 1999 (1999-04-29)  STRAUSBERG R.: "Homo sapiens cDNA  clone IMAGE:2239185 3' similar to  SW:PAK3_Human 075914  serine/threonine-protein kinase."  XP002169314  abstract  DOC. AGAINST INV.110 (SEQ.IDs. 231, 113)</p>	1,2,4-7, 10-14
P,X	<p>NAGASE T. ET AL.: "PREDICTION OF THE  CODING SEQUENCES OF UNIDENTIFIED HUMAN  GENES. XV. THE COMPLETE SEQUENCES OF 100  NEW CDNA CLONES FROM BRAIN WHICH CODE FOR  LARGE PROTEINS IN VITRO"  DNA RESEARCH,  vol. 6, 29 October 1999 (1999-10-29),  pages 337-345, XP000865804  ISSN: 1340-2838  -&amp; DATABASE EMBL 'Online!  Accession Number AB033090,  11 November 1999 (1999-11-11)  OHARA O. ET AL.: "Homo sapiens mRNA for  KIAA1264 protein."  XP002169637  abstract  DOC. AGAINST INV.110 (SEQ.IDs. 231, 113)</p> <p style="text-align: center;">-/--</p>	1-14

# INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! Accession Number H29272, 19 July 1995 (1995-07-19) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:49948." XP002169315 abstract DOC. AGAINST INV.111 (SEQ.IDs. 232, 114) ---</p>	6,7
P,X	<p>WO 99 64589 A (ZENECA LTD) 16 December 1999 (1999-12-16)  the whole document DOC. AGAINST INV.111 (SEQ.IDs. 232, 114) DOC. AGAINST INV.112 (SEQ.IDs. 233, 115) ---</p>	1-14,23, 26-30, 35-38
X	<p>DATABASE EMBL 'Online! Accession Number AA098024, 27 October 1996 (1996-10-27) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:550913 5' similar to SW:DROME P18475 tyrosine-protein kinase receptor torso precursor." XP002169442 abstract DOC. AGAINST INV.112 (SEQ.IDs. 233, 115) ---</p>	1-4, 6-13,23
X	<p>DATABASE EMBL 'Online! Accession Number Z98752, 23 August 1997 (1997-08-23) RAMSAY H.: "Human DNA sequence from clone RP1-138B7 on chromosome 20q13.12." XP002169443 nts. 43893 - 62413 DOC. AGAINST INV.113 (SEQ.IDs. 234, 116) ---</p>	1-14
X	<p>DATABASE EMBL 'Online! Accession Number AF035013, 4 January 1999 (1999-01-04) JIANG Y. AND ZHAO K.: "Homo sapiens cell cycle related kinase mRNA, complete cds." XP002169444 abstract DOC. AGAINST INV.114 (SEQ.IDs. 235, 117) -----</p>	1-14,24

# INTERNATIONAL SEARCH REPORT

International application No.  
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## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☒ Claims Nos.: 31-34  
because they do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
~~use of FURTHER INFORMATION in the application~~ PCT/US 01/010
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
- X
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: 1-19 (partially), 20 and 22 (completely), 23-38 (partially), 39 and 40 (partially), 41 and 42 (partially), 43 and 44 (partially), 45 and 46 (partially), 47 and 48 (partially), 49 and 50 (partially), 51 and 52 (partially), 53 and 54 (partially), 55 and 56 (partially), 57 and 58 (partially), 59 and 60 (partially), 61 and 62 (partially), 63 and 64 (partially), 65 and 66 (partially), 67 and 68 (partially), 69 and 70 (partially), 71 and 72 (partially), 73 and 74 (partially), 75 and 76 (partially), 77 and 78 (partially), 79 and 80 (partially), 81 and 82 (partially), 83 and 84 (partially), 85 and 86 (partially), 87 and 88 (partially), 89 and 90 (partially), 91 and 92 (partially), 93 and 94 (partially), 95 and 96 (partially), 97 and 98 (partially), 99 and 100 (partially).
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: Claims 1-14,26-38 (all partially)

A nucleic acid molecule encoding a kinase polypeptide as represented by SEQ.ID.122 or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by SEQ.ID.122 or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide as represented by SEQ.ID.122.

2. Claims: Inventions 2-78: Claims 1-20,  
23-38 (all partially and as far as applicable)

A nucleic acid molecule encoding a kinase with a polypeptide sequence selected from SEQ.IDs.123-199, wherein invention 2 is limited to SEQ.ID. 123, invention 3 is limited to SEQ.ID. 124, ....., and invention 78 is limited to SEQ.ID.199, or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by a polypeptide sequence selected from SEQ.IDs.123-199 or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide represented by a polypeptide sequence selected from SEQ.IDs.123-199.

3. Claims: Invention 79: Claim 21 (completely) and Claims  
1-14,26-38 (all partially)

A nucleic acid molecule encoding a kinase polypeptide as represented by SEQ.ID.200 or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by SEQ.ID.200 or a fragment thereof; an antibody or antibody fragment having

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide as represented by SEQ.ID.200.

4. Claims: Invention 80: Claim 22 (completely) and Claims 1-14,26-38 (all partially)

A nucleic acid molecule encoding a kinase polypeptide as represented by SEQ.ID.201 or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by SEQ.ID.201 or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide as represented by SEQ.ID.201.

5. Claims: Inventions 81-121: Claims 1-20, 23-38 (all partially and as far as applicable)

A nucleic acid molecule encoding a kinase with a polypeptide sequence selected from SEQ.IDs.202-242, wherein invention 81 is limited to SEQ.ID. 202, invention 82 is limited to SEQ.ID. 203, ....., and invention 121 is limited to SEQ.ID.242, or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by a polypeptide sequence selected from SEQ.IDs.202-242 or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide represented by a polypeptide sequence selected from SEQ.IDs.202-242.

6. Claims: Inventions 122-136: Claims 15-20, 23-25 (all partially) and claims 1-14, 26-38 (if applicable)



FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

A nucleic acid molecule encoding a kinase polypeptide as represented by a 'gene name' selected from 'AA980090', 'AA045601', 'AA297313', 'N23936', '5R72-18-1', '5R79-54-1', '5R65-16-1', 'AA065538', 'H17727', 'W08549', 'AA430250', 'AA139478', 'R87679', 'W65887', 'AA948538', '5R69-23-3', and '5R69-26-2', wherein invention 122 is limited to 'AA980090', invention 123 is limited to 'AA045601', ..... and invention 136 is limited to '5R69-26-2', or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide encoded by said nucleic acid molecule or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a said polypeptide.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 31-34

The search was based on the sequence listing furnished in computer readable form, the numbering of which differs from the numbering in the figures.

Claims 31-34 refer to a 'substance that modulates the activity of a kinase' without giving a true technical characterization. Moreover, no such specific compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT).

No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. l. Application No

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